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REGULATION AND THE QUALITY OF MEDICAL CARE*

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IN THE present state of confused thinking about new plans for distributing adequate medical care it seems that sufficient attention has not been paid the important fact that *medical care can be prescribed only by physicians*. The scope of even the most elaborate system of medical care is limited by the capabilities of the doctors participating in it. Up to the present time no carefully co-ordinated effort has been made to inquire whether or not patients, under the present voluntary system of medical care, are obtaining the maximum benefits possible from the skill of physicians. It is logical that such an inquiry be made before any radical new system is introduced. By the same token, should economic and social pressures force the adoption of a new system of medical practice or some modification of the old, much thought needs to be given to the means of utilizing the capabilities of physicians in the most efficient manner possible. In this paper some of the factors that are at present impairing the efficiency of physicians in their efforts to distribute good medical care are discussed together with a plan that may aid in the resolution of some of them.

Most physicians undoubtedly are sincerely anxious to give the best possible medical care to their patients, but there are many hindrances in this direction. Some of these are due to methods of practice established by tradition, some to lack of continuing educational opportunities for practicing physicians, some to the competitive nature of medical practice, and some to the ignorance of patients regarding health, disease and methods of treatment, and, unfortunately, a few are due to the black curses of all professions: unethical activities and frank malpractice. Many of these factors have served to create professional animosities and to discourage initiative in developing needed reforms in methods of practice or extensions of medical facilities. If some of these hindrances could be removed or reduced, the results would immediately be felt in improved medical care, but if sufficient attention is not given to their abatement, any new plan of distributing medical care will be forced to function at a level considerably below the possible maximum.

Among the traditions of medical practice that have not kept pace with modern needs and that in some ways have led to practices that are not always in the best interests of patients is the custom of fixed fees for office and home visits by the physician. Minimum flat-fee schedules have by custom been adopted by most local medical societies to forestall ruinous price-cutting competition. These fee schedules have become so ingrained in community thinking that at present the public resists any individual efforts at change. Because patients have not been adequately educated to the tremendous importance of careful and extensive examinations, physicians may be tempted to adopt short cuts to diagnosis and treatment. The discipline of careful study of each case, so arduously learned in medical school and internship, is gradually slackened bit by bit until in some cases much of it is gone forever. The worst offenders are those who attempt to handle a large practice by making snap diagnoses and by giving routinized treatments.

Another unfortunate custom is the demand that *some* treatment be given to nearly every patient, based upon the public's belief — which is not discouraged — that there is a treatment for every ill. (How many millions are needlessly spent by patients, who experience discouraging frustrations seeking treatments that do not exist?) This is closely allied to the custom, still widely practiced, of dispensing medication. These customs, together with relatively low flat-fee schedules, have encouraged the practice of giving unnecessary treatments or the treatment of patients without any serious effort to establish a diagnosis. Much of the unnecessary treatment being given is due to improper diagnosis, to the lack of any diagnosis (symptomatic treatment) or to attempts to make diagnoses on the basis of response to treatment. Doctors are therapeutically minded and thus are easily led astray by premature claims of therapeutic successes. The total cost of unnecessary treatments must be considerable, particularly when much of it is given

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in the form of proprietary preparations. Included under the heading of unnecessary treatment is the practice some doctors have adopted of seeing a patient frequently — but for only a short time at each visit, at which some treatment is usually given — in the hope of hitting upon the correct diagnosis eventually. Instead, if at the first visit they would take the time necessary to obtain a complete history and to do a complete physical examination, the diagnosis might be apparent.

In attempts to circumvent the fixed-fee tradition some doctors have adopted as a means of profit the practice of using diagnostic tests they are not qualified by training or experience to use, such as the electrocardiograph, office x-ray study and clinical laboratory examinations, all of which may be performed in a substandard fashion. Many of these deviations from good medical practice occur when men delude themselves into believing they are practicing "scientific" medicine. Unfortunately, their mistaken diagnoses often cause harmful procrastination in instituting curative therapy, or they may initiate needless and serious neuroses in their patients.

The tradition that the doctor is all things — medical and surgical — has led some physicians into the serious pitfall of attempting surgical procedures far beyond their capabilities. There is no doubt that unnecessary surgery has been done and in some areas is still being done. Here again the relatively low fixed-fee schedules for medical examinations and treatments have by contrast undoubtedly been responsible, at least in part, for increasing the attractiveness of high-fee surgery. In parts of this country privately owned hospitals are still in abundance, and most of them are owned by surgeons, or by groups largely dependent upon the surgeons' incomes. Their hospital operating deficits, which are almost inevitable if adequate care is given, are more than compensated for by the professional surgical fees. The only controls on the quality of surgery in most private hospitals, and in poorly directed nonprofit hospitals as well, are the consciences of their surgeons. It is in these hospitals that much of the unnecessary and misdirected surgery is being performed. Fortunately the efforts of the American Medical Association, the American College of Surgeons and other societies to reduce the opportunities of unqualified surgeons are showing real results.

The great discrepancy between the relatively low fixed-fee schedules of general practitioners and the large fees patients are willing to pay to specialists has, of course, tempted some doctors into setting themselves up as specialists without the necessary qualifications. The serious results of this practice cannot be measured. These pseudospecialists at times are apt to prescribe unorthodox, unnecessary and expensive treatments in attempts to appear unusually brilliant. Ideally, a specialist should only see patients in consultation with or at the request of a family doctor. On the other hand, pseudospecialization has encouraged what has now become a widespread but unfortunate practice — namely, that of competition between "specialists" and general practitioners. Patients, instead of turning to a family physician first for advice in all medical matters, often attempt to diagnose their own ills to the extent of selecting the proper specialist to confirm the diagnosis and to carry out the treatment. The growth of group practice has occurred partially in response to patients' demand for care by specialists. All of this has unnecessarily increased the costs of medical care and has created a tendency in practitioners to avoid sending patients to consultants for fear of losing them entirely.

General practitioners rightly believe that competition between them and specialists or groups is eminently unfair. In many communities this type of competition has created professional animosities, which at times are so strong as to hinder the execution of good medical care. Many general practitioners become intellectually frustrated because only the routine and least interesting cases are entrusted to their care. One consequence of this is that general practice is attracting fewer and fewer young doctors, and some are predicting the early demise of the general practitioner. To many doctors group practice is becoming more and more attractive because in group practice the stimulus of seeing unusual cases helps to forestall intellectual frustration and in most groups there are opportunities for pursuing a specialty. The American Specialty Boards have made inroads in reducing pseudospecialization but the uneconomic trend toward a state in which all medical care will be handled by specialists remains unslackened. The recently established American Academy of General Practice may aid in reversing this trend.

The lack of continuing educational opportunities for physicians is another factor that impairs the efficiency of doctors.* To keep abreast of developments in medicine in its present dynamic state, physicians must constantly be exposed to continuing educational experiences, not only through the medium of medical-society meetings, journals or formal postgraduate courses given at medical centers, but also in their contacts with colleagues and patients in the hospitals, each hospital being, in a sense, potentially a teaching institution. It should be the responsibility of those best able to assume direction — the faculties of medical schools — to enter into the teaching programs of all hospitals. Unfortunately, until recently most medical schools have not recognized this obligation to their graduates, with the result that the medical knowledge of some doctors is outdated to an unfortunate degree. Some of these men have through long years of faith-

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ful community service achieved positions of prestige. Naturally, they assume a defensive attitude toward efforts to change the *status quo* in methods of medical practice, for they fear that their deficiencies, real or imagined, would be brought to light under any regulated program. Age and experience should be powerful assets to any doctor, but for them to be maximally useful a co-ordinated plan of continuing education is essential.

Some of the deleterious competitive practices that have crept into the system of medicine as it now exists have already been mentioned. In a competitive society it would be almost impossible to eliminate them entirely, but when it can be shown that they may interfere with the welfare of patients, every effort should be made to reduce the more serious practices to a minimum. Although standards in some private hospitals are excellent, substandard medicine is practiced in many of them. It has been observed that competition is most apparent in areas where privately owned hospitals are numerous. The large overhead of a private hospital creates the need for a large volume of practice, with a rapid turnover of patients, so that the maximum income from professional fees may be obtained. There is therefore always the temptation to solicit patient business without too much regard to the maintenance of ethical relations with physicians who do not send patients there. The likelihood that such hospitals may be utilized for the performance of misdirected surgery has already been noted. At times, different groups in two or more private hospitals are competing against each other in the same area. This results in the division of doctors into several camps that rarely interchange ideas and seldom work together in the best interests of the people of their community. Much less of this competitive feeling is apparent in sections served by well run, nonprofit community hospitals open to all ethical physicians.

Public knowledge concerning health and disease has increased tremendously during the past generation through education, but many misconceptions are still prevalent. For example, because he has never been educated along these lines the average patient has little or no idea of how to select a family doctor or of how much to rely upon a specialist's opinion. Similarly, an appreciable number of people place their lives in the hands of medical cultists without realizing the vast gulf between the low quality of medical care practiced by this group and the high quality offered by competent physicians. Some patients "shop around" from one doctor to another because of preconceived notions about possible diagnoses and treatments. Other examples of pitfalls encountered by patients because of ignorance are too numerous to mention. What is necessary is a well organized authoritative program of public education and the development of some means of enabling patients to judge the competence of physicians. An informed public can be the strongest possible stimulus for keeping doctors abreast of the times.

Frankly unethical practices and malpractice need not be discussed here inasmuch as methods for their control through medical-society censure and legal proceedings are already quite effective.

It is significant that the highest quality of medicine is practiced in hospitals where rigid regulations governing the activities of the staff are in effect. Short cuts to diagnosis, unnecessary treatment, misdirected surgery, pseudospecialization and other mediocre practices are not countenanced. Mistakes in diagnosis and treatment are openly discussed in order to lessen the likelihood of their recurrence. Regular participation in continuing educational activities is encouraged for all staff members. The spirit of co-operation between doctors is highest in communities with first-rate community or teaching hospitals. Unfortunately, the fine example set by these centers has not as yet served to close the wide gap between the best medical care and the average now generally available. On the other hand, the quality of medical care probably drops to its lowest ebb in areas where the activities of the staffs of community and private hospitals are poorly regulated.

If some acceptable form of regulation could be applied to all doctors in somewhat the same manner as in teaching and well run community hospitals, the quality of medical care would surely improve everywhere. Because of the traditional freedom from encumbrance they have enjoyed in the past, even simple regulations may seem distasteful to doctors. This is an era of change, however, and the alternatives to self-regulation may be even more unpleasant.

Certainly, most members of the medical profession and a great many nonprofessional people as well would agree that the power of regulating the quality of medical care should not be vested in the federal Government because of the manifest dangers of inflexibility and political domination. It should be obvious as well that the increased demands for medical attention that would develop under an obligatory system of medicine would only serve to foster many substandard medical practices. Some have suggested control through more stringent state licensing regulations, with the necessity of meeting certain requirements at regular intervals. Here again there is the danger of political interference with the patient-physician relations. Also, how can the worth of a physician to his community be measured by unimaginative examinations?

On the surface it might seem logical that local, state and national medical societies, which have already done much to improve medical standards, should expand their efforts still further. The Council on Education and Hospitals of the American

Medical Association has made great strides in improving the standards of medical education by the application of rigid regulations to medical schools and hospitals serving as centers for intern and resident training. Because of these regulations, the undergraduate and formal graduate training of physicians in this country is of the highest order. There are, however, no similar regulations governing the practice of medicine once the training period has been completed. Likewise, the regulations do not apply to the many hospitals unable to meet the Council's standards. Patients treated in these hospitals have no way of gauging the quality of the medical care they receive. The American Specialty boards, sponsored by the American Medical Association and various specialty societies, have helped immeasurably in setting high standards for physicians desiring to qualify as specialists. The Boards regulate just a fraction of the entire profession, however, and with only minor exceptions they exercise no regulatory functions once certification has been granted. Also, the existence of the specialty boards has tended to divert young men from general practice and has discouraged attempts by general practitioners to prepare themselves for specialties while engaging in practice. The American Academy of General Practice has recognized the importance of giving special recognition to general practitioners who are conscientious enough to devote at least one month to approved formal postgraduate study every three years. This society has taken the forward step of controlling its members by renewing memberships at three-year intervals, and then only if the postgraduate stipulation has been met.

The American Medical Association and other national and state societies have sponsored additional programs that undoubtedly are contributing to the improvement in the quality of medical care. All these efforts have aided in establishing American medicine at the high point it has reached today, particularly in the teaching centers. None of them, however, seem capable of eliminating the faults in medical practice previously enumerated, and none have been directed specifically against these problems. In fact, they seem to heighten the contrast between the medical care offered in teaching centers and that in nonteaching areas.

Further regulatory steps by existing societies would probably prove to be difficult, because, to be effective, they would undoubtedly require the mobilization of public opinion. This is ethically distasteful, and in any event, public opinion has already been adversely influenced by the injurious propaganda of the proponents of compulsory health insurance who have labeled organized medicine as reactionary.

It appears that a new, unbiased and dynamic force needs to be introduced — a force free of reaction and political control and one capable of commanding public confidence. Such a force could be created through the medium of a privately financed organization headed by civic and professional leaders of national reputation. It would be the sole function of this organization to co-ordinate all present efforts aimed at improving the quality of medical care and, when necessary, to seek out new methods. For example, such an organization could conduct a program of public education that might help immeasurably in breaking down some of the barriers to the proper distribution of good medical care, particularly those that have been created by traditional methods of practice such as the fixed-fee system. Also, through education, patients could be taught to demand that thorough examination be completed before treatment is begun, since treatment without diagnosis is often useless and may be harmful, and that all surgery be performed by properly qualified surgeons in approved hospitals and then only after appropriate diagnostic study. Patients could be encouraged to consult a family physician first regarding all medical matters rather than to shop around for specialists. To carry through this idea some method would have to be devised to aid patients in selecting their doctors. Perhaps a certificate could be granted for display in the offices of doctors whose professional standing is acceptable to other doctors as well as to prominent lay advisers of each community. Under such a program, doctors whose efforts to pursue some special interest are ethically and morally correct would be encouraged even though their training did not qualify them for the more rigid American boards. Perhaps further stimulation could be achieved by the requirement that these certificates be renewed at stated intervals, depending upon postgraduate study and other activities in the interval. Such a certificate, if its importance were properly publicized, could be withheld from unqualified persons and thus act as a deterrent to those who attempt to use diagnostic instruments for profit, to pseudospecialists or to those who try to do surgery beyond their capabilities. There would have to be regional advisers selected from leading members of the medical profession to make suggestions with an eye on local needs and problems. What would be frowned upon in a metropolitan area might because of necessity be perfectly acceptable in a remote community. Thus, there would be no rigid national program, but rather a very flexible set of standards that could easily be changed with changing conditions. Doctors whose qualifications failed to meet minimum standards — and because of the need to explore this field cautiously at first this group would undoubtedly be relatively small — would be encouraged to attend approved postgraduate courses in medical centers to improve their knowledge and thereby to achieve certification. Government or private aid to finance these men during their courses

of study could be sought. A survey of the needs for high-standard diagnostic centers and community hospitals could be made, and suggestions given regarding the raising of funds for their establishment. Advice and direction could be given to boards of trustees of existing community hospitals and private hospital groups about methods for improving and maintaining standards. The organization could also serve those interested in setting up prepaid or labor-union health programs of high quality. Finally, further checks in addition to these already in operation could be applied to control unethical professional activities.

The mere existence of such an organization would do much to discourage shoddy practices. Civic, labor and professional groups would be stimulated to survey their own local needs and seek means for satisfying them. The leaders of the medical profession would certainly approve the establishment of an organization devoted solely to the improvement of medical care, and undoubtedly would co-operate in the setting up of advisory committees. There is no reason for this organization to supersede societies already engaged in improving the quality of medical care since its work would enhance their constructive activities. Under whatever system of medical practice that evolves from the present transition, the existence of an organization of this type would protect the best interests of the public, and it stands to reason that the great majority of practicing physicians would welcome a service that should aid in breaking the shackles of tradition that have encouraged deceit.

To be successful, a new national organization of this type would need a mandate from the grass roots of the medical profession — county or local medical societies, hospital staffs and even less closely knit groups, all of which must recognize that it should be possible to improve the quality of medical care in all areas without regimentation. Expressions of acceptance of these principles from many widely scattered areas would demonstrate an awareness of the need for some type of regulation such as has been outlined and a willingness to sacrifice some prerogatives to achieve greater efficiency. Such a demonstration should be of interest to those who cherish a voluntarily regulated system of free enterprise.

It is not beyond the realm of possibility that through such an organization the very large segment of the medical profession that believes medicine to be a responsibility rather than a trade would achieve unity and soon find a solution to the difficult problem of ensuring everyone medical care of *high quality*.

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THE CLINICAL IMPORTANCE OF COAGULASE-POSITIVE, PENICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS**

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PENICILLIN-resistant *Staphylococcus aureus* has been isolated with increasing frequency since the introduction of this agent in 1941. Rammelkamp and Maxon[1] tested 29 strains of *Staph. aureus* in 1942. All were inhibited by low concentrations of penicillin on initial isolation, but resistant organisms appeared in 4 cases after the administration of the drug. During 1943, Spink and his associates[2] reported 12 per cent of 68, and Rantz and Kirby[3] 26 per cent of 43 strains to be penicillin resistant. Kirby[4] recovered similar organisms from 7 patients, none of whom had received penicillin.

Gallardo,[5] in 1944, tested 85 strains of coagulase-positive *Staph. aureus*, of which 12 per cent were resistant. A year later Plough[6] noted that 40 per cent of 40 strains were penicillin fast, but only 1 was recovered before therapy was begun. Harley and his associates,[7] reporting from a war zone in India, isolated no penicillin-resistant *Staph. aureus* from patients with late, infected compound fractures who had not received this drug. A similar group receiving penicillin yielded 9.4 per cent penicillin-insensitive staphylococci. Many such strains were recovered from wounds secondarily infected in hospitals. Blair et al.[8] tested 79 cultures of *Staph. aureus* in 1945 and noted that 17, or 21.5 per cent, were insensitive to penicillin.

Barber and Rozwadowska-Dowzenko,[9] in a recent study of *Staph. aureus* infections, observed a progressive increase in the yield of penicillin-resistant strains from 14 per cent in 1946 to 59 per cent in 1948. Hirsh et al.[10] reported 4 cases of bacteremia or endocarditis due to penicillin-resistant, coagulase-positive *Staph. aureus*. In each case resistance developed after penicillin therapy was begun. Nichols and Needham,[11] early in 1949, reported 34 of 50 recently isolated strains, or 68 per cent, to be penicillin-resistant.

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Methods

Sixty-four strains of coagulase-positive *Staph. aureus* obtained from as many patients and isolated from clinical materials between August, 1948, and May, 1949, were tested. Penicillin sensitivities were determined by streaking eighteen-hour broth cultures of the organisms on horse-blood-agar plates in which varying amounts of penicillin were incorporated. The usual concentrations employed were 0.05, 0.1, 0.2, 0.4, 1, 2, 5, 10, 20, 50 and 100 units per cubic centimeter. Complete absence of growth was chosen as the end point. This method has been found to be simple and reliable in this laboratory and by Simmons and Christie.[12] Strains of *Staph. aureus* requiring 0.4 unit per cubic centimeter or more for inhibition were considered resistant.

Records of patients from whom *Staph. aureus* had previously been recovered and tested for penicillin sensitivity were also studied.

Nasal cultures were obtained from a number of healthy infants and children in the outpatient clinic, and from members of the house staff and laboratory personnel. When strains of coagulase-positive *Staph. aureus* were recovered, their penicillin sensitivity was determined by the technic described above.

Results

Sensitivity of Collected Strains

Interpretation of certain penicillin sensitivities determined several years ago was difficult because 0.1 unit of penicillin per cubic centimeter was the highest concentration employed in some cases.

Table 1. *Incidence of Penicillin-Sensitive and Nonsensitive Strains of* Staph. aureus (*1944-1949*).

Period	Total No. of Cases	Nonsensitive Organisms		No. of Sensitive Organisms
		No. resistant to penicillin	Growth in presence of 0.1 unit per cc.	
1944–1945	27	3 (11.1%)	6 (22.2%)	18 (66.7%)
1946–1948	29	13 (44.8%)	4 (13.8%)	12 (41.4%)
1948–1949				
Adults	30	18 (60.0%)	0	12 (40.0%)
Children	34	18 (52.9%)	0	16 (47.1%)
Totals (1948–1949)	64	36 (56.2%)	0	28 (43.8%)

Therefore, a special category of organisms, known only to be uninhibited by this amount of penicillin, has been organized (Table 1). The designation "not penicillin sensitive" encompasses this group of organisms, and the known penicillin-resistant strains that required 0.4 unit of penicillin per cubic centimeter or more for inhibition.

In 1944-1945, strains of coagulase-positive *Staph. aureus* from 27 patients were tested. Nine, or 33.3 per cent, were not penicillin sensitive, but only 3, or 11.1 per cent, of these were proved to be resistant. Values for the period 1946-1948 in 29 persons comprising this group were 58.6 per cent for nonsensitive organisms and 44.8 per cent for resistant staphylococci (Table 1). It must be emphasized that these data were obtained from selected patients, whose clinical status, such as the presence of a particularly severe infection or lack of response to therapy, indicated the need for sensitivity studies.

Table 2. *Relation of Penicillin Sensitivity to Recent Administration of Penicillin.*

Type of Organism	History of Recent Penicillin Administration	No History of Recent Penicillin Administration	Administration Undetermined
	No. of cases	No. of cases	No. of cases
1944–1945:			
Nonsensitive	7	0	2
Sensitive	1	14	3
1946–1948:			
Nonsensitive	7	4	6
Sensitive	1	9	2
1948–1949:			
Resistant	27	7	2
Sensitive	3	23	2

The recent (1948-1949) series was composed of 30 adults and 34 children. Eighteen (60 per cent) strains isolated from adults and 18 (52.9 per cent) obtained from children were penicillin resistant, a total of 36 (56.2 per cent), as demonstrated in Table 1.

There was a positive correlation between recovery of resistant staphylococci and the presence or absence of recent penicillin therapy (Table 2). Sensitive strains were rarely isolated from infections in persons who had received this agent. Conversely, recovery of resistant organisms from lesions in patients to whom penicillin had not been administered recently did not occur during 1944-1945, but was accomplished in a sufficient proportion (34.4 per cent) during 1946-1949 to indicate the presence of an important clinical problem.

Table 3. *Inhibitory Levels of Penicillin for 36 Strains of Penicillin-Resistant, Coagulase-Positive* Staph. aureus.

Inhibitory Level of Penicillin*	No. of Strains
unit/cc.	
0.4	1
1.0	4
2.0	3
5–10	9
25–50	11
More than 50	8

*22.2 per cent inhibited by 2 units or less; 77.8 per cent inhibited by 5 units or more.

Penicillin resistance was usually quite marked (Table 3). Only one of the resistant strains studied during 1948-1949 required less than 1 unit of peni-

cillin per cubic centimeter, and 78 per cent required 5 units or more for complete inhibition. Penicillin-resistant and penicillin-sensitive organisms were recovered concurrently in only 3 cases. Repeated testing of several strains confirmed their marked resistance, but variations were occasionally demonstrated in the concentration required for complete inhibition.

Relation of Resistance to Effect of Antimicrobial Therapy

Superficial lesions were the most common sites of infection by penicillin-resistant *Staph. aureus*, but there were many other clinical sources of these organisms (Table 4). No definitely adverse effects upon the course of local infections were attributable to penicillin resistance of the etiologic agent. Such processes usually responded to simple conservative management and surgical drainage. Penicillin resistance was an important factor in the course and management of 2 cases of sepsis due to *Staph. aureus* with bacteremia and 1 of meningitis caused by this organism.

TABLE 4. *Sources of Penicillin-Resistant, Coagulase-Positive Strains of* Staph. aureus *(1948-1949).*

SOURCE	NO. OF ADULTS	NO. OF CHILDREN	TOTAL
Blood	2	4	6
Local superficial lesions (abscesses, ulcers and so forth)	8	8	16
Urine	2	0	2
Abdominal sinuses	2	0	2
Bone marrow in case of osteomyelitis	1	0	1
Sputum in case of pneumonia	1	0	1
Ears	0	4	4
Eyes	1	1	2
Spinal fluid in case of meningitis	1	1	2
Totals	18	18	36

CASE 1.* A 23-year-old single man was admitted to the hospital on November 16, 1948. One or more furuncles of the buttocks had been noted about 2 weeks before admission but had subsided spontaneously. Two days before entry, headache, malaise and lethargy developed. A mild sore throat and vomiting appeared the next day. A private physician was called at this time. The patient was examined, 300,000 units of penicillin given, and he was immediately hospitalized.

The patient was semicomatose, irrational, and acutely ill on entry, with a rectal temperature of 38.4°C. (101.1°F.). The pharynx was moderately injected, and there were several small macular purpuric spots over the chest. Abdominal and Achilles reflexes were absent, the knee jerks were hypoactive, and bilateral Babinski signs were present. Fluid was present in both knees.

The white-cell count was 14,350, with 97 per cent neutrophils. Two spinal-fluid examinations on the day of entry revealed a cell count of 44 per cubic millimeter, with 93 per cent neutrophils and a + test for globulin, but organisms were not isolated. Coagulase-positive hemolytic *Staph. aureus* was isolated from the blood on November 16, 17, 18, 19 and 23, and from the knee fluid on November 20. This organism grew in the presence of 25 but was inhibited by 50 units of penicillin per cubic centimeter. It was sensitive to 5 microgm. of streptomycin per cubic centimeter.

*We are indebted to Dr. Eli Movitt, of the Veterans Administration Hospital, Oakland, California, for permission to include this case.

On the day of admission 5 gm. of sulfadiazine was given intravenously, followed by 2 gm. orally in 4 hours, and then 1.5 gm. every 4 to 6 hours. Penicillin, 50,000 units every 3 hours, and streptomycin, 4 gm. daily, were also begun. The penicillin was increased to 1,000,000 units every 3 hours on November 18, 2,000,000 units every 3 hours on November 23 and 4,000,000 units every 3 hours on November 24. Streptomycin and sulfadiazine were discontinued on November 23.

The course was one of continuous decline, with a persistently high temperature and bacteremia (Fig. 1). Purpura, a loud apical systolic murmur, and physical and roentgenographic evidence of pneumonia appeared. The patient died 10 days after admission to the hospital. Multiple abscesses of the brain, heart and kidneys, and acute bacterial endocarditis were discovered at autopsy. There was no response to combined antimicrobial therapy including sulfadiazine, streptomycin and massive doses of penicillin. It is probable that the penicillin resistance of the *Staph. aureus* was primarily responsible for the failure of treatment.

CASE 2. An 8-year-old boy was admitted to the hospital for the 3rd time on May 19, 1949, for treatment of recurrent laryngeal papillomas. Previous therapy had been only temporarily beneficial, and a tracheotomy had been required during a previous admission. There was a history of a congenital cardiac anomaly, probably a tetralogy of Fallot. A Blalock operation had been successfully performed in October, 1946, at this hospital.

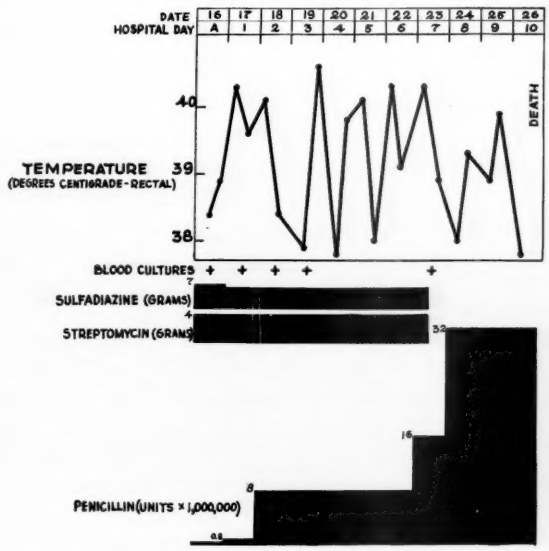

FIGURE 1. *Fatal Penicillin-Resistant* Staph. aureus *Sepsis with Bacteremia (Case 1).*

Direct laryngoscopy was done under general anesthesia on the day after entry, a laryngeal biopsy was performed, and the remaining papillomas touched with podophyllin. The course was uneventful for the following 2 days, but a moderate cough and rise of temperature to 39.7°C. (103.5°F.) occurred on May 22 and a few coarse rales were heard posteriorly at the left base. Intramuscular administration of procaine penicillin, 300,000 units daily, was started at this time.

Fever persisted, and the blood was cultured on May 24. Coagulase-positive *Staph. aureus*, resistant to 200 units of penicillin per cubic centimeter but inhibited by 10 microgm. of streptomycin and 0.1 microgm. of aureomycin per cubic centimeter, was recovered. The same organism was isolated from the blood on May 26, 29 and 31 and on June 2 and 3. It required 25 microgm. of streptomycin per cubic centimeter for inhibition on May 29, and it grew in the presence of 50 microgm. per cubic centimeter on May 31.

A throat culture performed on May 26 had revealed coagulase-positive *Staph. aureus*, but only the usual nasopharyn-

geal flora was present on June 3. The total white-cell count on May 25 was 10,400, with 84 per cent neutrophils. The urine was normal. Roentgenographic evidence of pneumonia was not obtained on May 26.

The antimicrobial therapeutic regimen is presented in Figure 2. Penicillin and dihydrostreptomycin were administered concurrently in increasing amounts to 3,500,000 units per day of the former, and 4 gm. per day of the latter, without significantly altering the course of the disease or eliminating the bacteremia. Aureomycin and sulfadiazine were then given and increased in amount to 2 gm. of the former and 4 gm. of the latter per day. Clinical improvement began within 48 hours of the addition of these agents. Bacteremia persisted for 72 hours; subsequent blood cultures were sterile. The temperature was normal within 5 days, and uneventful recovery followed.

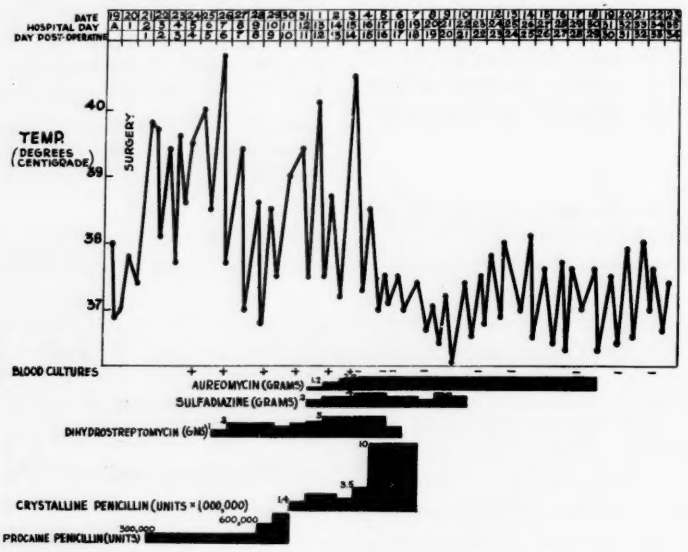

FIGURE 2. *Penicillin-Resistant* Staph. aureus *Sepsis with Bacteremia Successfully Treated with Antimicrobial Agents (Case 2).*

This was a case of penicillin-resistant *Staph. aureus* sepsis with bacteremia. In view of the cardiac history, endocarditis or endarteritis was considered. The laryngeal operative wound was the probable portal of entry, since this organism was present in the throat early in the disease.

Penicillin and streptomycin, given simultaneously, failed to affect materially the course of the illness. The slight diminution in temperature between May 26 and 31 may have been the result of the administration of the latter drug. It is of interest that an elevation of temperature coincided with the development of streptomycin resistance by the organism recovered from the blood. Response to the addition of combined aureomycin and sulfadiazine therapy was good; negative blood cultures were obtained within four days, and complete defervescence occurred within six days of their institution. Credit for the clinical effect cannot be assigned with certainty to any agent since four antimicrobial drugs were given concurrently. The possibility of additive or even synergistic action by the various chemicals must be considered. Comparison of this case with Case 1 suggests that aureomycin was the effective drug since the principal difference between the therapeutic regimens was the addition of this agent in Case 2.

CASE 3. Ventriculography was performed in a 7-year-old boy with a neoplasm of the third ventricle on March 7, 1949. Irregular fever, with temperatures as high as 39.5° C. (103.1°F.), had been present for the preceding 6 months. The spinal fluid was sterile on March 12, 1949, but coagulase-positive strains of *Staph. aureus* were recovered from it on March 13, 14 and 15. The organism was resistant to penicillin and sensitive to streptomycin; 1,650,000 units of penicillin had been administered before this organism was isolated. Streptomycin was first given on March 15. Staphylococci were not recovered subsequently from the spinal fluid. Within the next 3 weeks 42.5 gm. of streptomycin and 9,500,000 units of penicillin were administered. The fever gradually subsided, but death occurred on April 17 as the result of increasing intracranial pressure. A third-ventricle ependymoma and minimal evidence of meningitis were found at autopsy.

Other Cases

Penicillin-resistant and streptomycin-resistant strains of *Staph. aureus* were recovered twice from subdural fluid in a patient who had undergone craniotomy about one week earlier and in whom an enterococcal brain abscess was demonstrated later. The role played by the staphylococcus was uncertain.

Only one positive blood culture was obtained in 4 cases, early in the illness in each. One patient was a child with acute lymphatic leukemia who rapidly succumbed to multiple severe hemorrhages and bacteremia due to *Escherichia coli*. Another child with acute lymphatic leukemia had a submandibular abscess from which penicillin-resistant

strains of *Staph. aureus* were recovered two weeks after the single positive blood culture had been obtained. Two patients were clinically much improved before receiving penicillin. All these cases were probably examples of transient bacteremia due to *Staph. aureus*.

Healthy Carriers

Coagulase-positive strains of *Staph. aureus* were recovered from the external nares of 34 healthy infants. Penicillin-resistant strains were isolated from 10 of these subjects — an incidence of 29.4 per cent. There was no history of previous penicillin administration in 8 of the 10 cases. Data were not available concerning the other 2. As newborn infants, all patients had been confined in hospitals one to six months before being examined. Only 4 of the 19 house-staff and bacteriologic-laboratory members yielded coagulase-positive *Staph. aureus* on nasal culture. Three were carriers of penicillin-resistant *Staph. aureus* exclusively. A mixture of resistant and sensitive organisms was present in the other.

Sensitivity of Penicillin-Resistant Strains to Other Antibiotics

The streptomycin and aureomycin sensitivities of a number of penicillin-resistant strains of *Staph. aureus* were determined by plate methods. One organism was moderately resistant to streptomycin, requiring 25 microgm. per cubic centimeter for inhibition. All the others were sensitive, being inhibited by 5 microgm. of streptomycin and 1 or 2 microgm. of aureomycin per cubic centimeter.

Discussion

The data accumulated in this study confirm the observations of Barber and Rozwadowska-Dowzenko[9] and Nichols and Needham,[11] and further emphasize the fact that there has been a steady increase in the relative number of infections caused by penicillin-resistant strains of *Staph. aureus*.

Some difference in opinion has arisen regarding the origin and transmission of penicillin-resistant *Staph. aureus*. North and Christie[13] demonstrated that penicillin-sensitive and penicillin-resistant strains successively recovered from the same person were of the same bacteriophage type. They concluded that the resistant organisms were composed of descendants of the sensitive parent strain. Barber and Rozwadowska-Dowzenko[9] noted a similar chain of events but also, on two occasions, isolated resistant *Staph. aureus* whose type differed from that of the original sensitive organism. Miller[14] has suggested that resistant bacteria readily act as secondary invaders of infections in patients treated with penicillin. The observation of Harley and his associates[7] that hospital infection of wounds provided the highest incidence of penicillin-resistant *Staph. aureus* supports this view. Hospital cross-infection was apparently responsible for over half the cases of Barber and Rozwadowska-Dowzenko[9] yielding penicillin-resistant *Staph. aureus* in which the drug had not previously been given.

Of the nasal carriers reported here, 29.4 per cent yielded penicillin-resistant *Staph. aureus*. None of these healthy subjects had received penicillin, but most were in recent contact with hospital environments. Martyn[15] recovered penicillin-resistant, coagulase-positive *Staph. aureus* by nasopharyngeal culture from 56.5 per cent of 81 healthy newborn infants. None had received penicillin, but all were in a hospital.

The question must immediately be raised whether the present high incidence of infection by penicillin-resistant *Staph. aureus* is of serious clinical import. Strains of this organism that have been made insensitive to the action of the drug in vitro are of low invasiveness and have characteristics different from those of the parent organism.[8, 16] This is not so when the organisms have been isolated in cases of human disease. Investigation of experimental infection in mice has demonstrated that such staphylococci are capable of producing fatal illnesses that are not favorably altered by the administration of penicillin.[13, 17]

Few reports have appeared describing therapeutic failures as the result of infection by penicillin-resistant *Staph. aureus*. Twelve of 15 successive examples of staphylococcal sepsis with bacteremia, recently studied by Nichols and Needham[11] at the Mayo Clinic, were caused by highly penicillin-resistant staphylococci. The course of these illnesses was not affected by the usual amounts of penicillin. Similarly, this agent was ineffective in the 2 cases of staphylococcal sepsis described above. Furthermore, it is of importance to note that the organism was isolated from the blood on 7 occasions during the period of this investigation; 6 of the isolated strains were resistant to penicillin. The remaining examples of serious staphylococcal disease described in this paper do not permit an evaluation of the effect of the penicillin resistance of the etiologic agent on the efficacy of therapy with this antimicrobial agent. Barber and Rozwadowska-Dowzenko[9] have described 2 cases of fatal sepsis caused by *Staph. aureus* with bacteremia, in both of which intensive penicillin therapy was ineffective. In 1 case renal insufficiency led to the development of penicillin blood levels of 8 units per cubic centimeter. A similar unfavorable result was obtained by McLetchie[18] in 2 cases of pneumonia due to penicillin-resistant *Staph. aureus* in infants.

Information presently available does not indicate that the "wild" staphylococci carried by the population at large are frequently resistant to penicillin. It is clear, however, that persons who have received this drug, or who have been hospitalized or in contact with hospital environments, are likely to harbor resistant staphylococci or to suffer in-

fections caused by them. It is of the greatest importance that penicillin-sensitivity tests be carried out during the study of infections that develop in patients in any of these categories. If this is not done, valuable time may be lost in the treatment of a disease with penicillin, which will then be proved to be useless.

Investigation for the purpose of determining the efficacy of other antimicrobial agents in the treatment of staphylococcal disease caused by penicillin-resistant organisms is obviously of the greatest importance. Nearly all such strains that have been studied have been inhibited by low concentrations of streptomycin.[9] The 2 cases described above demonstrate that this agent may not be particularly effective in the management of serious staphylococcal sepsis. Rapidly developing bacterial resistance to the drug will doubtless be the cause of failure in most cases. Studies in this laboratory and by Lankford and Lacy,[19] as well as by Nichols and Needham,[11] indicate that penicillin-resistant staphylococci will be readily inhibited by aureomycin in vitro. The latter investigators have reported the successful treatment of 4 out of 6 generalized staphylococcal infections with this drug. A similar case is described above. Not yet evaluated is the possible role of combined antibiotic therapy in such cases. Concurrent administration of aureomycin and streptomycin may well be of value, since the latter agent might be expected to inhibit the growth of highly streptomycin-resistant mutants as they appear, in addition to having striking antibacterial action in itself.

Summary

Fifty-six per cent of 64 strains of coagulase-positive *Staphylococcus aureus* obtained from clinical material between August, 1948, and May, 1949, were penicillin resistant.

There was a close correlation between the isolation of resistant strains and previous administration of penicillin, but 20 per cent were recovered from persons in whom this drug had not been given.

Thirty per cent of strains of *Staph. aureus* isolated from the noses of healthy children who had not received penicillin were resistant to this agent.

Two cases of sepsis caused by *Staph. aureus* with bacteremia, in which massive penicillin therapy was inefficacious, are reported.

The possible role of other antimicrobial agents in the treatment of penicillin-resistant staphylococcal infection is discussed.

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STUDIES IN ACUTE CHOLECYSTITIS*

II. Cholecystostomy: Indications and Technic

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CHOLECYSTOSTOMY has become an unwanted stepchild in the family of surgical procedures. Its presence as a recognized operation is admitted, but its legitimacy is suspect. In the standard textbooks of surgical methods[1-3] the technic is but sketchily outlined, and then as a procedure carried out under general anesthesia with a full gall-bladder incision. The operation is usually mentioned as a means of escaping from a technically difficult situation by a relatively simple procedure. It has its proponents,[4-6] but it is often regarded as an operation suitable for the timorous or inexperienced but rarely carried out by the skillful surgeon.

It is the purpose of the present communication to reaffirm the value of this simple technic in certain cases of acute cholecystitis. We believe that at times it is a life-saving procedure to be carried out as a planned operation under local anesthesia, and that it is not to be reserved merely as a means of escape from a technically difficult situation.

MATERIAL

In a recent communication[7] the experience with acute cholecystitis at the Peter Bent Brigham Hospital during the years 1941-1947 was recorded. During this period 649 patients underwent operations for biliary diseases exclusive of cancer or stricture of the bile ducts. There were 6 deaths — a mortality of 0.9 per cent. One hundred and thirty-four of these patients suffered from acute cholecystitis, and 2 of the 6 deaths occurred in this group — a mortality of 1.5 per cent. Cholecystostomy was performed on 20 patients, or 14.9 per cent of the acute group. Two of this group had a second cholecystostomy for recurrent acute cholecystitis after intervals of eighteen months and four years respectively. The 2 deaths from acute cholecystitis were in the cholecystostomy group — a mortality of 10 per cent for this procedure (Table 1).

Of the 20 patients undergoing cholecystostomy, 5 represent cases in which the surgeon resorted to drainage of the gall bladder as a means of getting out of a difficult situation. In 4 cases the local situation was so difficult, with inflammatory adhesions, edema and, in 2 cases, abscess formation obscuring the anatomic landmarks, that the operator chose merely to drain the gall bladder and close the wound. In the other case the patient was explored through a lower abdominal incision because of the mistaken diagnosis of appendicitis. In this patient, a man of seventy-nine with generalized peritonitis, acute cholecystitis with perforation was discovered at the time of operation, and rather than prolong the procedure to a significant degree, cholecystostomy was performed. This patient eviscerated on the tenth day and died two weeks later of overwhelming sepsis with the Welch bacillus.

TABLE 1. *Results of Operation in Acute Cholecystitis (Peter Bent Brigham Hospital, 1941-1947).*

OPERATION	NO. OF CASES	NO. OF DEATHS
Cholecystectomy	64	0
Cholecystectomy and choledochostomy	50	0
Cholecystostomy	20	1
Second cholecystostomy	2	1
Cholecystectomy after previous cholecystostomy	6	0
Cholecystectomy and choledochostomy after previous cholecystostomy	6	0
Totals	148*	2 (1.5%)

*There were 134 patients.

In the other 15 cases (11.2 per cent of all cases of acute cholecystitis) cholecystostomy was performed as a planned procedure under local anesthesia because of the severity of the illness or serious intercurrent disease that made it evident that any attempt at definitive surgery would entail an unwarranted degree of risk to the patient. Of these 15 patients, the youngest was fifty-three, and the oldest eighty-two years old; the average age was sixty-seven and a half, and the mean age seventy. Four were jaundiced, and 7 had palpable gall bladders. All but 4 were women. Eight of them had some serious metabolic disorder or significant cardiovascular disease. All were sick, febrile and toxic. Three of these patients had no further surgery. Two had second attacks of acute cholecystitis after intervals of eighteen months and four years respectively and required second cholecystostomies. The second of these died of pulmonary embolism seventeen days after the second cholecystostomy at the age of seventy-eight. Ten of the 15 patients had definitive surgery performed some days or weeks after the cholecystostomy. In 5 of these the common duct was explored. None of these patients died.

The high mortality following cholecystostomy is attributed to the gravity of the disease and should not be interpreted as an indication of the

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inadequacy of this procedure. The patients who succumbed after cholecystostomy could not have been saved by cholecystectomy. Moreover, if cholecystectomy had been undertaken initially in the other complicated cases, the gratifyingly low mortality of 1.5 per cent for the entire series could not have been attained.

Indications

As has been intimated, cholecystostomy is carried out under two sets of conditions: because of unexpected technical difficulties that are found in a patient despite general anesthesia and an adequate incision; and, secondly, as a planned procedure under local anesthesia because of the precarious condition of the patient.

Technical difficulties forced the surgeon to resort to cholecystostomy in 5 out of the 134 cases. It is impossible to describe exact criteria for arriving at the decision to abandon a planned cholecystectomy. It is obviously based to a large degree on the skill and experience of the surgeon. The beginner may meet this situation frequently, and the master surgeon of many years' experience very rarely, but inevitably there will be some patients in whom the anatomic landmarks are so obscured by inflammatory reaction that a stubborn persistence in the attempt to remove the gall bladder will endanger the patient's welfare. The hazards are twofold. In the first place, to persist in an attempt to remove the gall bladder under difficult circumstances may result in inadvertent trauma to the common duct. On the other hand, the surgeon may be influenced to leave behind a considerable segment of cystic duct or even some of the ampulla because of his fear of damaging the common duct or hepatic artery. It is well known that the inadequate removal of the cystic duct may be a source of postcholecystectomy symptoms.[8] It is our contention that it is far better in the occasional difficult case to consider cholecystostomy as the first stage of a two-stage cholecystectomy than to persist in an extremely difficult dissection that may either endanger the patient's life or health or lead to an inadequate operation and a poor symptomatic result. Further discussion of this matter is useless because in the last analysis only the surgeon at the operating table can make the decision. It should be made only on the basis of the difficulties encountered, and not through any false sense of pride.

As pointed out elsewhere,[7] the ideal treatment of acute cholecystitis is prompt cholecystectomy, with exploration of the common bile duct as indicated. Unfortunately, however, delay in hospitalization, difficulties in establishing the diagnosis and the poor general condition of the patient make this impossible in approximately 50 per cent of the cases. In the majority of the advanced or complicated cases judicious delay will allow a definitive operation to be performed in a few days. But in about 20 per cent of these cases (10 per cent of all cases of acute cholecystitis), the patients are so ill or the disease is so fulminating that delay is impossible. It is under such circumstances that a planned cholecystostomy is the procedure of choice.

In this series cholecystostomy was carried out in 15 patients as a planned procedure under local anesthesia. In general it may be said that these patients were so sick either from the fulminating character of the cholecystitis or from some serious intercurrent disease that any extensive operation would have been a definite threat to life itself. Cholecystostomy under local anesthesia is so simple that it adds nothing to the hazards confronting the patient, and it abruptly checks the toxic, febrile course. Definitive surgery may then be carried out later when the patients are in the best possible condition, or it may be postponed indefinitely in certain cases in which the associated diseases are so severe that any elective operation is inadvisable.

There are some specific indications for cholecystostomy and some that are less exact. The specific indications are as follows:

Decompensated heart disease. In the presence of acute cholecystitis there is not time to treat the heart condition effectively, and cholecystostomy is the procedure of choice. Three of the cases fell in this category.

Diabetes. In patients with acute cholecystitis and uncontrolled diabetes, regulation is difficult if not impossible until the acute infection has been controlled by drainage of the obstructed gall bladder. There were 2 such patients.

Other severe intercurrent disease. This includes any condition that makes major surgery hazardous. In the group under consideration there was 1 case of uncontrolled pernicious anemia and 1 of bilateral pleural effusion (cause undetermined) and 1 patient who had had a major cerebral vascular accident just a few days previously.

A less precisely defined but equally important group comprises patients who are fairly sick and toxic on admission but who rapidly worsen despite supportive therapy in the hospital. Many of the older patients with acute cholecystitis are quite sick when first seen and exhibit fever, rapid pulse, dehydration and generalized evidence of toxicity. However, the majority of these improve quite rapidly when their fluid balance is restored, antibiotics are started and general supportive measures employed, so that definitive surgery may be performed without undue risk. Nevertheless a small group remains in whom the signs of toxicity rapidly increase despite the use of similar supportive measures. In these patients the pulse, temperature and white-cell count rise, the abdominal signs in-

crease, there may be evidence of peritonitis, abscess or significant jaundice, and it soon becomes evident that they will never be candidates for definitive surgery and, indeed, their lives are threatened unless the toxic course is interrupted. About half the cases of planned cholecystostomy fall in this group, and it is in these patients that the most careful observations and judgment must be exercised by the responsible surgeon. The clinical course of these patients has been well described by Zollinger[9] in a previous communication from this hospital.

Age per se is not an indication for cholecystostomy. Most of the patients requiring this operation are in the older age group, but a young patient with decompensated heart disease or diabetes in addition to fulminating acute cholecystitis may require cholecystostomy. On the other hand, many patients of advanced age are perfectly good candidates for definitive surgery. Age is a potent secondary factor in the decision to perform cholecystostomy, but it is not the primary consideration.

To summarize, cholecystostomy under local anesthesia is indicated when the patient's general condition is so poor that definitive surgery is hazardous. The poor condition of the patient may be due to severe intercurrent disease or to the severity of the cholecystitis itself. The remarkably low mortality from acute cholecystitis at the Peter Bent Brigham Hospital is attributable in considerable degree to the judicious employment of cholecystostomy in the desperately ill patient.

Technic

The operation can easily be carried out under local anesthesia. The seventh through the eleventh intercostal nerve on the right side is blocked in the mid-axillary line with 2 cc. of 1 per cent procaine solution for each nerve. In addition, the abdominal wall is locally infiltrated with procaine at the site of the incision. The location of the incision is important. Usually in these elderly people, even though they are obese, the musculature of the abdomen is not heavy, and the fundus of the swollen gall bladder can be palpated. If this is not possible, one may assume that the point of maximum tenderness represents the inflamed fundus touching the undersurface of the peritoneum. It frequently happens that after the premedication and the intercostal block have taken effect, the gall bladder previously hidden by protective muscle spasm can be accurately palpated. For this reason the surgeon should always carefully re-palpate the abdomen just before making the incision. The fundus may be surprisingly low in the abdomen. A transverse or oblique incision about 5 cm. long is made 1.5 cm. or so cephalad to the most prominent point of the gall bladder (Fig. 1*A*). This allows the fundus to be sutured to the peritoneum at the close of the procedure without undue tension. The incision is made without regard to any landmarks other than the gall bladder; the fascia and muscles are cut in the direction of the fibers, and the peritoneum opened (Fig. 1*B*). The gall bladder presents itself immediately as a swollen, mottled, red or bluish-red structure, or there may be actual areas of gangrene. No attempt to explore the abdomen is made. Two stay sutures about 2 cm. apart are passed through the wall of the gall bladder to steady it. Any attempt at this stage to grasp the fundus with instruments is apt to tear the friable walls of the organ. The wound is protected with packing, and a trochar is then introduced between the two sutures and the bile is aspirated (Fig. 1*C*). This collapses the tensely distended organ, which retracts upward and immediately becomes much easier to handle. The trochar is withdrawn, and the hole is enlarged by excision of a crescent-shaped piece of the wall (Fig. 1*D*). This serves the double purpose of giving tissue for pathological and bacteriologic study and affording an adequate opening for subsequent manipulation. A culture of the bile is made.

Unless the gall bladder is gangrenous, it is now possible to grasp the margins of the opening with Allis forceps without tearing the tissues. Scoops are introduced, and the stones evacuated. Regardless of how many stones there may be, there is practically always a single stone impacted in the ampulla. This stone is often a basic mechanical cause of the disease. It is usually larger than the other stones, or it may be the only stone present. The index finger of the left hand is then introduced into the gall bladder and by palpation and gentle manipulation against a scoop held in the other hand it is usually possible to dislodge and withdraw the offending calculus (Fig. 2*A*). One should attempt to demonstrate the flow of normal-appearing bile back through the cystic duct. By this means the surgeon is certain that his decompression has been adequate (Fig. 2*B*). Occasionally, a flow of normal bile is not evident, and in such cases one must assume either that there is another stone lower in the ampulla or, if the patient is jaundiced, that the common duct is blocked by stone or an inflammatory mass proximal to the junction of the common and cystic ducts. One should not prolong the manipulation at this time, but unless normal bile appears during the early postoperative period, the decision to perform a second definitive operation may be made sooner than would otherwise be possible. Contrariwise, if large amounts of bile drain through the cholecystostomy opening and continue to do so for an indefinite period, it is evident that the common duct is obstructed distal to the junction with the cystic duct.

At this stage of the procedure the gall bladder is vigorously irrigated with saline solution to wash out small calculi, detritus and blood clots (Fig. 2*C*). A catheter is then sewn into the opening in the

gall bladder. A good-sized mushroom catheter with the end cut off is very satisfactory for this purpose. A suture is passed through the wall but not the lumen of the catheter and is continued as a pursestring suture closing the opening in the gall bladder snugly around the catheter (Fig. 2*D*). This suture is rolled inward by a second pursestring suture, which does not pass through the catheter (Fig. 2*E*). The fundus is then sutured to the undersurface of the peritoneum, usually by one suture at each quadrant. The original traction sutures may be used for this purpose. It has been said that suturing the fundus to the peritoneum causes discomfort from dragging on the peritoneum, but this has not been so in the cases of this series, and it seems preferable to block any possible pathway for leakage of bile around the tube into the peritoneal cavity. The wound is then loosely closed around the catheter with interrupted sutures (Fig. 2*F*). A drain is not necessary, the catheter itself serving as a drain for the wound.

It is usually unnecessary to look at the outside of the gall bladder except where it is exposed at the fundus. In a few of these cases there was free bile in the peritoneal cavity, and we found small necrotic areas leaking bile down near the ampulla. It is difficult to close such areas with sutures. By mere approximation of a bit of omentum, these defects apparently rapidly healed once the organ was adequately decompressed by the drainage tube. In other cases the omentum was already plastered to the outside of the gall bladder, and dissection

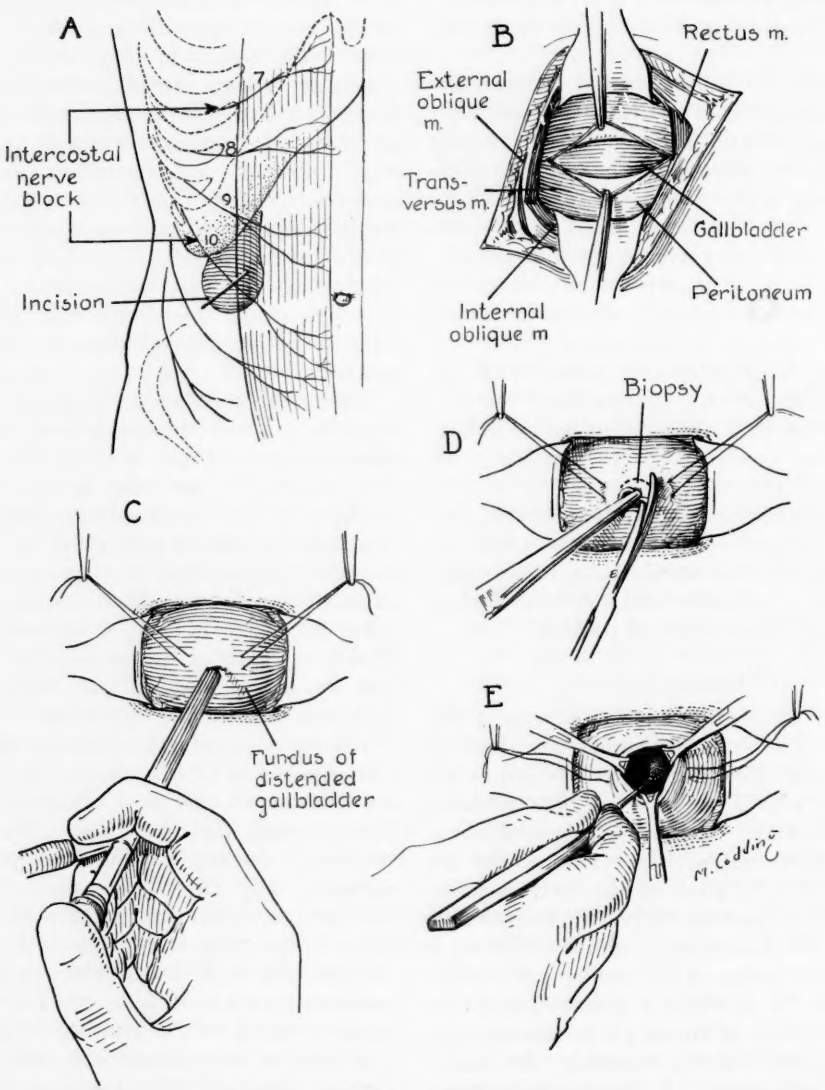

FIGURE 1. *Technic of Cholecystostomy.*

of this would probably have revealed small openings that were already sealed off.

Postoperatively there is an abrupt drop in pulse and temperature. A sense of well-being returns, and the patient is usually hungry the next day. The tube is left in place for seven to ten days and then removed unless there is very profuse drainage of bile. Before the tube is removed a cholecystocholangiogram should be taken to determine the patency of the cystic and common bile ducts.

The cholecystostomy should be regarded as the first stage of a two-stage cholecystectomy and is essential for the permanent well-being of the patient. Occasionally, however, advanced age and concomitant diseases make it reasonable to postpone cholecystectomy indefinitely provided that no obstruction to the cystic or common bile duct has been demonstrated by a cholecystocholangiogram. If the cystic duct is not patent, the cholecystostomy sinus will not heal, or if it does, recurrent pain, swelling and infection will follow. An obstruction of the common duct, of course, makes definitive surgery imperative.

The time at which definitive surgery is done will vary with the degree of local inflammation found at operation and the need for time to improve the patient's general condition. One month after the first stage is a reasonable time of election for the

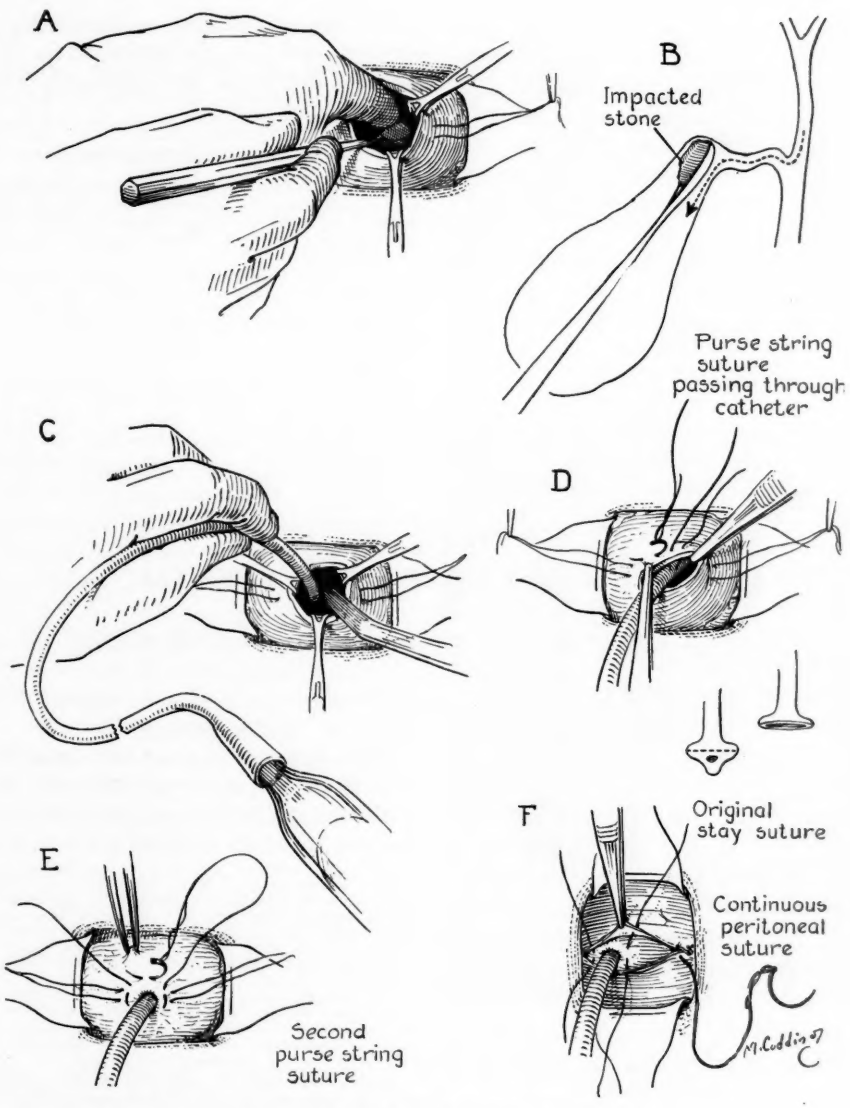

FIGURE 2. *Technic of Cholecystostomy.*

definitive operation. Occasionally it can be done in two weeks. Rarely the patient's general condition will require delay of longer than a month.

Of the 20 patients who had cholecystostomy in this series, 12 had subsequent cholecystectomy performed, and in 6 of these the common duct was explored. None of the 12 patients died. Four of the 8 patients in whom cholecystostomy only was performed remained well for periods of four years. In 2 patients no follow-up information is available. The 2 remaining patients entered the hospital with recurrent acute cholecystitis. One of these, an eighty-two-year-old woman, returned with a recurrent attack only four months after cholecystostomy. A second drainage of the gall bladder was done, but despite the recurrent attack, no further surgery was felt advisable because of advanced coronary-artery disease. This patient had no further gall-bladder symptoms for eighteen months, when she died of coronary thrombosis. The second patient with recurrence was seventy-four years of age at the time of the initial operation. She remained well for four years and then re-entered the hospital with another acute episode. A second drainage of the gall bladder was done under local anesthesia, but the patient died on the sixteenth postoperative day of pulmonary embolism after what had been an apparently uneventful convalescence.

If one elects to postpone definitive surgery, the chances of the patient's remaining free of subsequent attacks for several years seem to be about 50 per cent. Under such circumstances there should be strong reasons for recommending that operation be postponed.

Summary

Cholecystostomy is a life-saving procedure in certain cases of acute cholecystitis. The indications for this operation are discussed, and the technic is illustrated.

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OUTBREAK OF SMALLPOX IN A HOSPITAL

Lieutenant Colonel Hartwin A. Schulze, U.S.A.F. (M.C.)*

ON JANUARY 15, 1947, the Army Hospital at Wiesbaden, Germany, received a patient with the presumptive diagnosis of smallpox. The patient, a War Department civilian employee, was transferred by ambulance from an American dispensary at Liége, Belgium. He had become ill on January 7, with symptoms of an upper respiratory infection. Three days later a macular rash on the face and a whitish enanthem on the buccal mucosa appeared. During the next few days the rash became generalized, and at the same time it became papular and then vesicular. Ten days after the beginning of his illness he presented the appearance shown in Figure 1.

The general symptoms and the morphology, evolution and distribution of the lesions were all typical of a moderately severe to severe case of smallpox. The diagnosis was presumptively confirmed by the finding of numerous Guarnieri bodies in a biopsy of one of the skin lesions.

Vesicle fluid dried on cotton swabs in phosphorus pentoxide tubes was sent to the Army Medical Center in Washington and to the Pasteur Institute in Paris for further confirmation. Both institutions confirmed the diagnosis.†

Although the patient had been placed in isolation from the start, on R + 12‡ another hospital patient manifested a rash resembling smallpox. This patient had been admitted for infectious hepatitis

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†The laboratory procedure employed at the Army Medical Center consisted in the inoculation of fertile hens' eggs with a suspension of dried vesicle fluid; the observation of characteristic lesions on the chorioallantoic membrane; the identification of the specific lymph substance of variola-vaccinia virus on the chorioallantoic membrane by complement fixation and the identification of the virus as variola on the basis of animal susceptibility tests.

The Pasteur Institute performed tests consisting of injecting an emulsion of dried vesicle fluid together with penicillin into the testicles of immunized and nonimmunized monkeys, with the production of a characteristic inflammatory reaction with the presence of inclusion bodies of the Paschen type in the nonimmune animal.

‡This article employs a method of designating time that has probably not been used heretofore in medical writing. It is the system originally used in military planning but now also commonly employed in describing military events. In this system all time is referred to in relation to the day of some crucially important event — for example, an attack. The day of such an attack is designated D Day. Events prior to and subsequent to this day are designated as D+ or D− a certain number of days, as the case may be.

If a certain objective is captured three days after the attack this day is referred to as D + 3. If the troops participating in the attack had to be in their assembly areas three days prior to the attack this day would be designated as D − 3.

In the following article the crucial time is the date on which the initial smallpox patient was admitted to the hospital. Many of the important epidemiologic events that followed must be considered in their time relation to this date. The date of the admission of the original patient is called the "reference day," designated "R day" (R standing for reference). Days subsequent to R day are designated R + the number of days, — for example, R + 2, — and days prior to R day are designated R minus the number of days — for example, R − 2. If the first secondary case occurred twelve days after the admission of the initial case, this date would be written R + 12. If this patient had originally been admitted to the hospital two days prior to the admission of the initial patient, this date would be written R − 2.

by transfer from another hospital on the same day as the original smallpox patient.

An infant born in the hospital on R − 2 and released on R + 13 was readmitted with vesicular lesions characteristic of smallpox on R + 15.

Another infant born in the hospital on R day and released on R + 15 was found to have a few vesicular lesions on R + 17. This baby was readmitted with a diagnosis of smallpox on the following day.

Immediate Control Measures

It was accordingly obvious that the smallpox virus had not been confined to the isolation section but had been spread to distant parts of the hospital and that it had been introduced into at least two homes in the Wiesbaden community.

On R + 18 the following control measures were instituted:

Vaccination of all hospital personnel and all patients either currently in the hospital or subsequently admitted.

Vaccination of all contacts made by the 2 infants in their homes.

Quarantine of all patients who had been in contact with these 3 secondary cases for a period of sixteen days.

Closing of the obstetric ward to new admissions.

Recall and quarantine of all military contacts who had been released from the hospital since R day.

Vaccination and daily observation of all nonmilitary patients who had been released from the hospital since R day.

Discharge of no patients except those returning to the Wiesbaden area until they could fulfill the following immunization criteria — that they had a vaccinoid or vaccinia reaction from the vaccination given in the hospital or an immune reaction in the presence of a definite scar from a previous vaccination.

Handling of all possible contacts having an undiagnosed fever as smallpox until the diagnosis was established.

Investigation

It was initially assumed that the 3 patients with secondary cases had become infected at about the same time. A search was accordingly made for a common factor in the hospital experiences of these patients. The investigation uncovered several possibilities. In the primary case and the first secondary case blood counts had been made on R day. One of the infant patients had had blood drawn for a count on this day also. The second infant was born on this day, but did not have a blood count. Further pursuit of this idea disclosed that the same laboratory worker had drawn all blood specimens. The sequence of drawing the specimens, however, could not be established. The possibility existed that the infection was spread by inoculation from a contaminated automatic stylet. Transfer of the virus by some fomite carried by the laboratory worker was another possibility. Support was lent to this hypothesis by the lack of isolation precaution exercised by the laboratory worker. On R + 5 she had set her equipment tray on the bed of the first smallpox patient. On this occasion the error was immediately corrected by a medical officer who chanced to see it, but it is possible that a similar error went uncorrected on previous occasions.

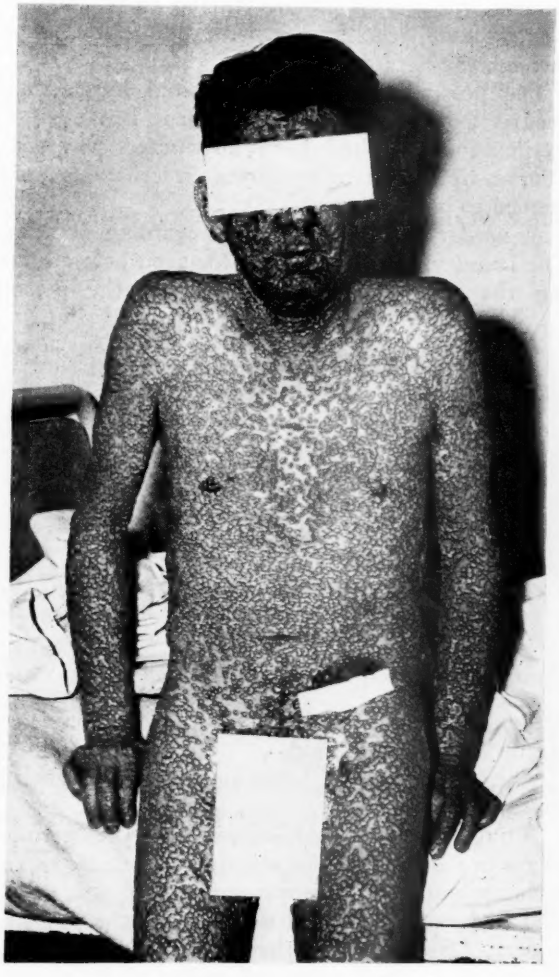

FIGURE 1. *Initial Patient on the Tenth Day after the Beginning of Symptoms. (Photograph Kindly Furnished by Signal Corps, United States Army.)*

Another possibility is connected with the night nursing supervisor. In addition to visiting all parts of the hospital it was her duty to administer whatever nursing care was necessary on the isolation ward since there was no night nurse assigned there. The initial patient was on the seriously ill list, and the nurse's notes indicate that she had adminis-

tered treatment to him on numerous occasions. On at least one occasion she had changed his bedclothes. During this process the virus-laden dust from ruptured vesicles that must have been dispersed would doubtlessly have thoroughly contaminated her in spite of mask and gown. This virus-infected dust could subsequently have been dispersed in the other wards she visited.

Although the night nursing supervisor's report included remarks regarding the obstetric ward nursery, she denied having entered there and admitted merely conferring with the duty nurse through the open door.

The possibility that contaminated hypodermic needles and other similar equipment had escaped sterilization and had been distributed was considered. The system employed in central supply seemed to preclude this.

A similar possibility existed regarding laundry. The laundry, however, was autoclaved before leaving the ward. Curiously, however, the person

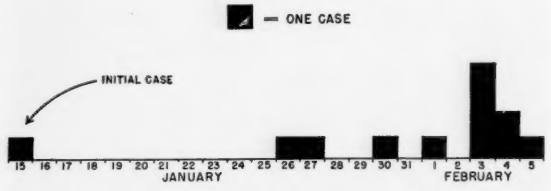

FIGURE 2. *Time of Onset of Symptoms of Smallpox in Patients in the Hospital Outbreak in Wiesbaden, Germany, January and February, 1947.*

normally responsible for this duty was on leave during the crucial period.

The sterilization of dishes and utensils seemed to be satisfactory.

A number of unskilled German employees were engaged in various types of cleaning operations on the isolation ward. They were required to wear gowns and had been instructed not to enter the patients' rooms. Observation of their activities made it apparent that they were unfamiliar with isolation technics and violation of the instructions must have been numerous. Besides, there were no safeguards to prevent them from visiting other parts of the hospital.

The possibilities of virus-laden dust moving in natural air currents or dust tracked on shoes were also considered. Nothing was done either to investigate or to minimize these possibilities. These factors perhaps merit further consideration.

Additional Secondary Cases

Between R + 19 and R + 23, 8 additional cases of smallpox developed. Five of these were in patients already in the hospital. One of these was a soldier who had been recalled from duty and placed in quarantine in the hospital because he was a contact with the first secondary case. His symptoms began three days after he was readmitted.

The other 4 were patients in widely scattered parts of the hospital. None of these had any known contact with the previous cases. They were distributed in the surgical, general medical, neuropsychiatric and prisoner wards.

Three of the patients were not in the hospital at the time they became ill. One of these, a woman who became ill on R + 19, had been a hospital patient from R + 2 to R + 9. While a patient she had been given fluids intravenously on numerous occasions and was routinely mentioned in the night nursing supervisor's report.

The other 2 were Negro soldiers from a battalion located about 10 miles from the hospital. The closest connection that could be established with the hospital was that one of them had on R + 6 attended a service theater in Wiesbaden. No one in the hospital admitted attending this same performance.

Figure 2 shows the time of occurrence of the cases based on the time of the beginning symptoms.

In addition to the 12 patients cared for in the hospital, 7 German civilians in the Wiesbaden area contracted the disease. The first occurred on R + 24 in the mother of a German girl employed in the isolation ward of the hospital as a nursing aide. The second reported case was in the mother of a German man employed as an attendant in the isolation ward of the hospital. Neither of these employees had themselves been ill. They had both been vaccinated shortly after the patient with the initial case was admitted. The third case occurred on R + 31 and involved the housekeeper in the home of a man employed on an outside detail of the hospital. The employee remained away from work from R + 18 to R + 20 because of an ill defined illness. He had no vesicular lesions but may have had a case of variola *sine eruptione*. He had a good vaccinia scar dating back eight years. He had been hired on R + 10. He had visited the hospital on R + 13 for a pre-employment examination and had returned on R + 15 for a blood test. This possible case is considered to be the fourth.

The fifth case occurred on R + 41 in a town contiguous with Wiesbaden. No connection could be established with any of the other cases. The sixth and seventh cases occurred between R + 60 and R + 65 in 2 persons living in the same house with Case 5.

Other Control Measures

The defects in isolation technics were corrected as they were found during the investigation that was made on R + 18.

Upon the occurrence of the first of the 2 cases in soldiers having no apparent connection with the hospital, the battalion from which they came was

vaccinated. At this time the battalion was about to move to an area about 100 miles southeast of Wiesbaden for the purpose of deactivation. The move was not prevented, but the battalion was put under quarantine upon arrival at the new location and dispersal of personnel delayed until expiration of the sixteen-day quarantine period.

On R + 27 it was decided to vaccinate all military persons and their dependents who lived in Wiesbaden. This was considered justifiable because it was known that the immunization status of military personnel and civilians in the theater was far from satisfactory. Besides, such action would help to sensitize the local doctors and the populace to the presence and the seriousness of the disease.

At the same time the Military Government Public Health Officer of Hesse urged the German public-health authorities to undertake a campaign for voluntary vaccination in the Wiesbaden area. This was done, but the extent to which it was carried out has not been determined.

The vaccinations carried out on military personnel and dependent from the time the first control measures were instituted were done with a fresh, locally produced vaccine of known high potency.

Previous Immunization

Immunization histories were obtained on the hospital patients by means of interrogation and search for vaccination scars. Army regulations require vaccination at the time of induction, within one year of going overseas and every three years thereafter. All patients gave a history of previous vaccination. Most of them had been vaccinated several times.

The assumption is that the majority of these recent vaccinations were unsuccessful. By detailed questioning about local manifestations following vaccination, coupled with the presence of scars or depigmented areas at usual vaccination sites, relatively accurate information was obtained concerning the time of the most recent *successful* vaccination. A verbal or recorded history of an immune reaction was disregarded because of the notorious unreliability of such information. These data are summarized in Table 1. It will be noted that there was a close relation between recent successful vaccination and the severity of the disease. This result was not influenced by vaccination after exposure since these vaccinations were done within three days of the first symptoms of the disease.

One of the infant patients had a mild case, exhibiting only about a dozen lesions. The mother had had a vaccinia reaction (pustule) from a vaccination in February, 1946. The other infant had a moderate case in which about a third of the skin surface was involved in the eruption. The mother had had an "immune" reaction in May, 1946. Although both mothers were exposed to their infants, neither contracted the disease. They both had immune reactions to the vaccinations given when their infants became ill.

Spread of the Infection

The occurrence of the additional cases in the hospital did not throw additional light on the possible manner of spread in the hospital. Neither did it serve to minimize or eliminate any of the possibilities considered at the start. The occurrence of cases in German civilians outside the hospital, through contact with German hospital employees, emphasized the lack of isolation control in the hospital but shed no light on the actual method of spread in the hospital. It seems likely that several methods of spread were involved.

Table 1. *Previous Successful Vaccination in Relation to the Severity of Disease in the Adult Smallpox Patients in the United States Army Hospital in Wiesbaden, Germany, January and February, 1947.*

Patient	Last Successful Vaccination		
	within 5 yr.	over 10 yr.	none
Mild cases:			
W. W.	?	?	?
D. S.	Yes (1946)	—	—
R. H.	Yes (1945)	—	—
W. D.	—	Yes (1930–35)	—
W. D.	—	Yes (1930–35)	—
J. S.	—	Yes (1934)	—
Moderate case:			
H. F.	—	Yes (1934)	—
Severe cases:			
L. E.	—	—	Yes
A. W.	—	—	Yes
R. A.	—	—	Yes
R. M.	?	?	?

Since there were no other cases of smallpox in this general region it is reasonably sure that all cases in the Wiesbaden area were derived from the original patient hospitalized there.

The initial case of the Wiesbaden series was apparently contracted in Paris. The patient had been in Paris between December 21 and 27. His symptoms began on January 7. This fits well with the usual twelve-day incubation period. Its origin in Paris, however, is obscure. No cases have been reported in the Paris region for many months. In February, however, an old man in the North Station–East Station district of Paris was diagnosed as having smallpox and, between then and April 10, 33 cases were reported, 2 of which proved fatal.[1] Smallpox had been present in North Africa throughout the previous year, and outbreaks had occurred in Spain, Portugal and Italy.[2] Since Paris is the greatest focal point for travelers in this part of the world, it is reasonable to assume that the disease was brought to Paris from one of these endemic centers, and that it smoldered in mild and unrecognized cases until identified in February. One theory advanced in France was that the virus was introduced with rugs imported from North Africa.

In April information was received that a smallpox outbreak was in progress in and about Liége, Belgium. In view of the fact that the first patient in the series of cases among American personnel was stationed in that city and was cared for in an American dispensary during the pre-eruptive stages of his disease, there was some speculation regarding the possible connection of the two outbreaks.

The answer to this question was received several months later in the form of a complaint coming through intergovernmental channels. Its substance was as follows:

> The Belgian Sanitary Service investigated an outbreak of smallpox that occurred in and about Liége and ascertained that the first case had occurred early in February "in the house of a worker in La Perle Laundry"; this laundry had as one of its customers an American medical dispensary; this dispensary, early in January, had treated an American War Department civilian employee for a condition that was diagnosed as smallpox and on account of which this patient was subsequently transferred to an Army hospital in Wiesbaden, Germany; the bedclothes used by this patient while he was at the dispensary in Liége had been sent to La Perle Laundry without prior sterilization.

According to the Epidemiological Reports of the World Health Organization, 21 cases of smallpox occurred in Liége during this outbreak.[3]

During the first half of 1947, 79 cases of smallpox occurred in England. The initial case, which occurred in February, came from Grimsby, a port city at which three vessels from France docked at about the same time as the beginning of the outbreak in Paris. This importation subsequently resulted in 48 cases. The second importation, which occurred in March, was from India and resulted in 31 cases.[4]

Summary and Conclusions

The admission of a smallpox patient in an Army hospital in Wiesbaden, Germany, was followed by the occurrence of 18 other cases.

Nine of these patients contracted the disease in the hospital. The contagion in 2 soldiers could not be traced to the hospital.

Seven German civilians contracted the disease. Four of these patients had direct or indirect connection with the hospital. The other 3 had no known connection with the hospital.

Because of the absence of other nearby foci of infection all cases in and about Wiesbaden were thought to have a common origin.

The manner of spread of the virus from the isolation ward was not completely ascertained, but transport of the virus on persons or fomites were undoubtedly involved.

The original case was probably contracted in Paris, where a small epidemic occurred a few months later.

The first American case was initially treated at a dispensary in Liége, Belgium. Because his bedclothes were sent to a civilian laundry without prior sterilization, another outbreak of smallpox occurred in that city.

The Paris focus was believed to have been responsible for 48 cases that subsequently occurred in England.

The vaccination program instituted after the development of secondary cases in the hospital outbreak, and perhaps the improvement of isolation procedures prevented the further spread of the disease.

Fomites, or mild, unrecognized transitory cases, or both, are an important source of spread of smallpox. Smallpox virus is a very durable substance for which ordinary isolation precautions are inadequate.

Many vaccinations against smallpox are worthless because of the employment of a poor technic or an impotent virus. A person having no vaccination mark or giving no clear-cut history of successful vaccination should show a pustular lesion six to twelve days after successful vaccination. If this does not occur, the vaccination should be regarded as a failure and vaccination should be repeated with a vaccine of known high potency and a faultless technic. An immune reaction (accelerated reaction in an immune person) cannot be distinguished from a "non-take" (vaccination failure) unless the site is examined on the second or third day after vaccination.

The diagnosis of smallpox should be attempted by laboratory means as soon as the suspicion of the diagnosis develops and should not await the occurrence of secondary cases.

I am indebted to Major Claude M. Eberhart, M.C., at the time epidemiologist in the Preventive Medicine Branch, Medical Division, Headquarters, European Command, and now of the Office of the Surgeon General, Department of the Army, who was of considerable assistance in the investigation of the hospital outbreak, and to Lieutenant Colonel Charles H. Moseley, M.C., public-health adviser to the Military Government of Hesse, who furnished the information concerning the case that occurred in the German civilian population.

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MEDICAL PROGRESS

PROCTOLOGY

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BOSTON

THIS report on progress in proctology concerns the following general subjects of interest: new books; anatomy; ulcerative colitis; complications of diverticulitis; perforation of the colon and rectum; unusual proctologic cases; megacolon; cancer; and publications of the American Proctologic Society and the Section of Proctology of the Royal Society of Medicine.

New Books

Three books on the subject of diseases of the colon and rectum have been published since the last review of proctologic subjects in the *Journal*. Late in 1948 a fourth edition of Gabriel's[1] *The Principles and Practice of Rectal Surgery* was brought out in this country as well as in England; this continues to be an excellent treatise on the subject. The author, who is well known to all who are interested in this type of surgery, was for many years an associate of J. P. Lockhart-Mummery at St. Marks Hospital in London and is now surgeon to the hospital, which is devoted entirely to the care of patients with diseases of the colon and rectum. The fourth edition of the book contains 278 illustrations and 494 pages of worthwhile material and is generally considered one of the best works on proctology.

Turell,[2] of New York City, has recently written a book covering the treatment of the common proctologic diseases. The volume includes a chapter on sulfonamide therapy, one on psychosomatic problems, and one on proctology in pediatrics, together with an enumeration of drugs and of instruments, some of which are original with the author. This should prove to be a useful work and is well illustrated.

A third edition, in two volumes, of Bacon's[3] book recently appeared. I have not yet had an opportunity to look over the new edition, but can say from my knowledge of the first two editions that this is undoubtedly the most comprehensive recent book on this subject and that it will be a valuable addition to the libraries of all whose interest lies along these lines.

Anatomy

Wilde,[4] of the Department of Anatomy of Manchester University, has made some interesting observations on anal and perianal anatomy, based on a dissection of freshly removed rectums from 12 adults and 8 fetuses. This article, which also summarizes and analyzes the observations of previous anatomists concerning this area, is well worth careful reading by anyone who is interested in the subject. It is well illustrated by photomicrographs and drawings, which are carefully described in the text. The author's conclusions, in detail, are as follows:

1. The internal sphincter is a pronounced thickening of the circular muscle coat, measuring 30-35 mm. in length and 5-8 mm. in breadth, in the adult.
2. The pecten zone is an area of transition between the rectal mucous membrane and the true skin. This region has its own macroscopical and microscopical characteristics and measures 15 mm. in breadth in the adult.
3. The longitudinal muscle coat fuses at the level of the deep external sphincter with the adjacent fibres of levator ani. The conjoint aponeurosis, so formed, becomes increasingly fibro-elastic as it descends.
4. The conjoint aponeurosis divides distally into a number of fibro-elastic cords that fan out to gain attachment to the anal skin over a broad area extending proximally to Hilton's line, and distally beyond the anal verge.
5. There is no evidence of any special thickening or aponeurosis in the position usually ascribed to the anal intermuscular septum.
6. Corrugation of the anal skin is an expression in function of the radiating septate structure of the termination of the longitudinal coat. There is no evidence for the existence of a separate corrugator cutis ani muscle as described by Ellis (1878), and it is believed that the fibres he figured were in reality elastic in structure and radiating from the terminal septa of the longitudinal coat.
7. It is suggested that the manner of insertion of the conjoint longitudinal coat affords ready passage to the skin of a low-level anal fistula. Furthermore, the subdivision of the perianal subcutaneous tissue into a honeycomb by tough fibro-elastic septa may explain the localization and painful nature of a haematoma following rupture of a vessel in the external annulus haemorrhoidalis.

In the 1949 *Year Book of General Surgery* 60 of the 575 pages are devoted to a review of articles pertaining to the colon, rectum and anus. Since these are readily accessible to anyone interested, only the five reviewed below are considered.

Ulcerative Colitis

Miller, Ripstein and Tabah,[5] in discussing the surgery of ulcerative colitis, emphasize the necessity for careful preparation of the patient before operation is undertaken. Ileostomy is their procedure of first choice, and colectomy is usually delayed for six months if possible, though in 6 cases they combined ileostomy with removal of the right colon as the primary procedure on the theory that they were thereby removing at the outset the part

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of the colon where the most absorption of toxic products occurs. At a later stage the left side of the colon is removed down to the sigmoid, with exteriorization of the remaining sigmoid end, or removal of the rectum and sigmoid by abdominoperineal resection as may seem best. These authors do not favor ileorectal anastomosis because the rectum is usually the most severely involved of any segment of the colon in this disease.

The Koenig–Rutzen bag is advocated as the best appliance for taking care of ileostomy drainage. In our locality, it is also agreed that this is the best ileostomy bag yet devised, because it can be cemented to the skin of the abdomen with a relatively nonirritating cement, fitting closely around the ileostomy, can be easily evacuated through a vent at the lower end of the bag and can also be removed for cleansing and reapplied once or twice a day without difficulty.

McKittrick and Moore,[6] reviewing the Massachusetts General Hospital experience in the care of this disease, stress the dependence of the patient on some member of the family, a friend or the doctor for a sympathetic understanding of the problems that must be met in living with the condition. These authors believe that an ileostomy, which is so important in the treatment of the disease, can very rarely be closed again with any expectation of permanent improvement in the colitis. They find that the patients who receive an ileostomy too early in the disease, before they have become sufficiently inconvenienced, never adjust themselves so well as those who are operated upon after the symptoms have become more pronounced. After a thorough course of medical treatment without improvement ileostomy should be carried out before the patient reaches a point at which his life is in jeopardy and his recovery doubtful. Colectomy must be performed if a fairly permanent, satisfactory response does not follow ileostomy. McKittrick and Moore make the statement that only one recurrence of an acute exacerbation after ileostomy should be permitted before colectomy is advised.

The statistics in this paper are as follows:

Of 149 patients with ulcerative colitis who had an ileostomy either initially, or as the only procedure, 22 died during the postoperative period. In most cases death was due, not to the ileostomy, but to progress of the severe colitis, often with perforation or hemorrhage, or both. Of this group of patients subtotal colectomy was performed in 87, with a 6.9 per cent mortality, and of the 87 patients the rectal segment was removed by combined abdominoperineal resection in 33, with a 3.3 per cent mortality. The subtotal colectomies were done at intervals of several months to twelve years after ileostomy. In reply to questionnaires sent to 110 patients who had ileostomy, 88 considered themselves in good health. Of the 110, 75 per cent believed that their working capacity had not been lessened, and 67 per cent believed that their social life had not been adversely affected.

Dunlop,[7] of Melbourne, Australia, makes a plea against the postponement of ileostomy because of the opinion of many physicians that it is undesirable. He emphasizes the fact that no permanent disturbance of electrolyte balance follows ileostomy, but that it is also true that ileostomy should not be performed unless medical treatment has failed and unless the patient gives evidence of going down hill or has serious complications. In his experience the ileostomy stools became thickened in a few weeks and usually semiformed in three months. He advocates a double-barrel ileostomy and advocates washing through the colon at intervals of one or two weeks unless the colon has been evacuating itself. Most of the surgeons in Boston and vicinity prefer a single-barrel ileostomy, with closure of the distal end of the ileum, which is replaced in the peritoneal cavity, and it is thought that irrigation of the colon is unnecessary and probably unwise.

Sanders[8] has applied, in 5 cases, the procedure of skin grafting a protruding ileostomy as suggested by Dragstedt. He cites as the greatest advantage of the method the absence of painful skin excoriations by avoidance of leakage on the surrounding abdominal skin. This method produces an epithelialized projecting spigot which empties well away from the abdominal wall, but the patient must wear suspenders, rather than a belt, and loose-fitting trousers to avoid injury to the protrusion. One wonders if a small, neat ileostomy with a Rutzen bag is not a better arrangement, though a prolapse may occur even when the ileostomy has been carefully constructed.

Dennis and his co-workers[9] report the result of vagotomy in 25 patients with ulcerative colitis. In 16, vagotomy was the only procedure. Of this latter group, 6 became symptom-free, 4 improved, 5 did not improve, and 1 became worse. The authors believed that the proctoscopic and x-ray evidence of disease had diminished and the character of the stools had improved after this operation. Three patients demonstrated complete loss of gastric acidity, and the others showed a marked reduction in free hydrochloric acid. One patient had gastric retention and required a later gastroenterostomy. It was the authors' opinion that the best chance of a good result could be expected when vagotomy was performed in the first few weeks of the disease.

McCready and his associates,[10] have furnished some concrete evidence regarding the nature and incidence of involvement of the ileum in chronic ulcerative colitis. Estimates of its frequency are reported by Crohn et al. as 8 per cent and by Bargen and Webber as 6.3 per cent.

This study is based on 23 post-mortem and 6 surgical specimens, a total of 29, in all of which the ileal involvement had developed secondarily to typical chronic ulcerative colitis. Great care was

taken to exclude any case of regional ileitis whose pathological picture is quite different, according to Mallory, from that seen in ileitis secondary to ulcerative colitis. The 23 cases were selected from a review of the autopsies in 81 cases, — an incidence of 28 per cent, — and the 6 surgical specimens constituted 27 per cent of 22 specimens removed at time of operation.

The pathological picture in 22 of the 29 specimens corresponded with that found in the colon — a complete, diffuse ulcerative process. But in the other 7 cases discrete ulcers were seen, with normal mucosa between. The process in the first group was undoubtedly a direct extension across the ileocecal valve, with actual linear ulcers crossing it, and the process was a severe one though less so than that in the colon. In none of the cases was the wall of the ileum thickened to the degree encountered in regional ileitis, and by the same token there was no stenosis. In the 23 post-mortem specimens at least 30 cm. of terminal ileum was involved in 6, and 45 cm. in 3. Also, of the 7 specimens with patchy ulcers, 3 had other areas of involvement in the upper ileum, and the other 4 revealed involvement of both ileum and jejunum. Perforation in the ileum occurred in 5 of the 29 cases; this is the most serious complication, for death almost inevitably results.

It was possible to make the diagnosis of ileal involvement by barium enema in 10 of 19 of these cases thus examined — just over 50 per cent. Of the 23 autopsied cases the ulcerative colitis was of the acute fulminating type in 8 and chronic in the other 15, so that ileal involvement is found in both types, and perforation occurred in only 1 of the acute type, the other 4 perforations being in the chronic group.

These authors suggest that despite the established dictum that handling of the bowel during operations for ulcerative colitis should be avoided as much as possible to prevent peritonitis and wound sepsis, it is nevertheless highly important to handle the ileum enough to be able to determine how high up the bowel should be transected to be above the involved area. One author even advocates incision and microscopical pathological examination at the operating table to be sure the point selected for ileostomy is definitely not inflamed.

Failure to place the stoma above the involved ileum is advanced as one probable explanation of the high mortality associated with ileostomy in the past, especially with operations performed as emergency procedures.

The incidence of carcinoma in association with ulcerative colitis has been discussed by many writers and has been reviewed again by Sauer and Bargen,[11] who have added 41 to 54 cases previously reported from the Mayo Clinic — a total of 95 cases. Of this new group of 41 patients about half were males, and the average age was forty-three and three-tenths years at the time of diagnosis. The average duration of the colitis before the diagnosis of carcinoma was made was sixteen years. In most patients there was enough change or increase in symptoms to suggest the onset of a new development in the course of the colitis. Multiple tumors were present in 12 cases, and associated polypoid changes in the mucosa in 24. The majority of tumors — 19 — were in the rectum, with 10 in the cecum as the next highest group. Tumors were palpable in 11 patients.

The lesson to be derived from a report of this sort is that all patients with ulcerative colitis whose colons have not been removed should be carefully watched in an effort to detect early manifestations of the onset of cancer in this disease.

Complications of Diverticulitis

Mayfield and Waugh[12] have studied 32 patients in whom sigmoidovesical fistulas due to diverticulitis existed, and have tried to analyze and evaluate the symptoms, pathological picture and operative findings in this group of cases, all of which were operated upon at the Mayo Clinic.

As a cause of sigmoidovesical fistula pelvic inflammatory disease had been placed first and diverticulitis second by one author who was quoted, but C. W. Mayo had found diverticulitis to be the cause in 59 per cent of a series of cases he had analyzed. It is also the opinion of most writers on the subject that diverticulitis is the most common cause.

The pathological picture was about what one would expect, with a fistulous tract of varying length, associated with abscess formation in 50 per cent of the cases, and unlined with epithelium in most cases except where a long diverticulum formed part of the tract. Of particular interest was the fact that in some cases in which a preliminary colostomy had been done twelve months or more before resection there was still evidence of perforation, abscess and necrosis. This is important evidence in favor of a more prompt and direct surgical attack on the lesion itself and raises doubt of the necessity or advisability of a preliminary colostomy and long period of waiting before resection of the affected segment in all cases. However, it is not stated in the article whether these preliminary colostomies were all of the type that accomplishes complete defunctioning of the left side of the colon or not. Presumably they were.

Of the symptoms, *pneumaturia* was the most constant, being present in 30 of the 32 cases, and 1 of the other 2 patients had passed barium in the urine although he had not noticed gas. Seventeen passed feces in urine, 18 had chills and fever, and frequency and dysuria were common symptoms. Pain was present in three fourths of the cases — in the lower abdomen or left lower quadrant.

The fistulous opening was visible on cystoscopy in 12 of 25 cases examined preoperatively, and in the other 12 cystitis, dimpling and granulation tissue compatible with fistula were observed. Pyuria existed in 31 cases.

Of the 32 cases, 30 were resected while the fistula was still present, 17 by an extraperitoneal type of operation, 12 by intraperitoneal resection with end-to-end anastomosis, and 1 by subtotal colectomy and ileosigmoidostomy. A catheter through the urethra was utilized in all but 6 cases in which suprapubic cystostomy was carried out at the same time as resection. Preliminary colostomy had been done in 19 of the cases, with an average elapsed time of fifteen months between procedures.

There were 3 deaths, a mortality of 9.3 per cent. Two patients died of peritonitis (1 also had pneumonia), and the third of gas gangrene after resection and end-to-end anastomosis.

In the follow-up study, 28 of the 29 survivors were cured of their fistula, though 1 had some sort of bladder disturbance later and 5 had some persistent pyuria.

Sigmoidovesical fistulas are not a common complication of diverticulitis, fortunately, but are a very important one to treat properly and cure. They are more common in men because of the presence of the uterus and adnexa between bladder and rectum in women.

In a series of 140 cases of diverticulitis that I reported in 1940 from the Massachusetts General Hospital there were only 4 cases of sigmoidovesical fistula.

In another article Mayfield and Waugh[13] made a study of 17 cases of sigmoidocutaneous fistula among 46 patients with diverticulitis who had some type of fistula formation, the remainder having bladder fistulas. Of these 17 patients 3 had coexisting enterocolic fistulas and 3 others vesicosigmoidal fistulas.

A brief review of the literature disclosed a few points of interest. One author reported that only 22 of 264 cases of fecal fistula studied were due to diverticulitis. In another series only 1 of 129 cases was due to diverticulitis. Transverse colostomy for three to twelve months prior to attempts at closure was usually recommended, but it was emphasized that a waiting period will often produce a closure without operation. On the other hand, surgical attempts to close the fistula gave a 31 per cent recurrence rate in a series of 28 cases.

In the group reported by Mayfield and Waugh 12 were males, and the leading symptoms were pain in the lower left or middle portion of the abdomen, with chills and fever in half the cases. None were obstructed in any degree. Fourteen had had a previous abscess with surgical drainage, whereas in the other 3 the external fistula followed operations for correction of sigmoidovesical fistulas. There was a single opening in 14 cases, and multiple openings in 3. The diagnosis of diverticulitis was confirmed by x-ray study in 14 of the 15 cases examined before operation.

These 17 patients were treated at Mayo Clinic by segmental resection with no mortality, and 16 were cured. Three cases, however, required a second operation for recurrence before the cure was obtained.

Lockhart–Mummery[14] reports an unusual case of localized diverticulitis of the transverse colon in a forty-eight-year-old woman operated upon with a preoperative diagnosis of acute appendicitis. A mass the size of a hen's egg was found in the colon about 6 cm. beyond the hepatic flexure, and the appendix was normal. The mass was then thought to be carcinoma, since it did not seem to be particularly inflamed, and it was resected by the Paul–Mikulicz method. The specimen, 15 cm. in length, contained only one diverticulum, 2 cm. in depth with a 3-mm. opening into the bowel lumen and with much surrounding edema and thickening. A later barium enema showed one large duodenal diverticulum and several ordinary diverticula in the cecum and ascending colon. Only one was visualized in the descending colon.

This case is of interest because it is quite uncommon for localized diverticulitis of the colon to occur elsewhere than in the sigmoid, and occasionally in the cecum. Only 1 other case report of such a localized process in the transverse colon could be found though Anderson, from the Mayo Clinic, had discovered 90 cases reported in other parts of the colon than the sigmoid.

Perforations of the Colon and Rectum

Pilcher[15] reports his experience in the care of over 200 cases of perforating war wounds of the colon and rectum. The author performed reconstruction operations in over half these cases and followed almost all through to recovery. In most, if not all, of the cases of injury to the colon the bowel was exteriorized rather than sutured, but the author does not believe that the Mikulicz type of closure of a double-barrel colostomy is so desirable as a complete resection of the spur with end-to-end suture of the bowel ends, after careful preoperative preparation. The bowel is then dropped into the abdomen, and a normal closure of the abdominal wall carried out. Pilcher also suggests that small perforations can probably be safely closed at the outset.

He emphasizes the importance, in wounds of the rectum, of a thorough abdominal exploration at the outset and a careful search to discover the full extent of the injury. If the rectal wound cannot be sutured immediately it should be treated by débridement and packed open and either sutured secondarily or allowed to granulate in.

Jones,[16] of Newcastle-upon-Tyne, found only 4 cases of traumatic perforations of the rectum in

civilian patients among 74,000 surgical admissions from 1938 to 1947. Two of these were due to perforations of an enema tip, 1 from a sigmoidoscopy, and 1 from impalement on a broom handle. He emphasizes the difficulty of surgical approach to the rectum in an effort to drain the perirectal tissue and advocates an incision parallel to the side of the sacrum and coccyx, dividing the fibers of the gluteus maximus near its origin and without removal of the coccyx. Another method is to make a curved incision just below the tip of the coccyx, with division of the fascia propria. If a perforation through either of these incisions can be found it should be sutured, but if there is difficulty about exposure, suture should not be attempted — a colostomy should be done, and the area drained from below. Diagnosis of intra-abdominal perforation rests upon the presence of abdominal pain together with x-ray evidence of free gas under the diaphragm. Coincident injury to the bladder can, of course, be ruled out by catheterization to determine the presence or absence of blood, or by cystoscopy if there is any doubt.

Although this type of lesion is fortunately uncommon it is very important to handle such an injury correctly and to estimate carefully the degree of injury and the organs involved at the outset.

I have had a case in which a boy was impaled on one of the rungs of a Windsor chair from which the top had been removed. This rung entered through the sphincter just at the left of the anus, passing upward through the pelvis outside the rectum, perforating the left rectus muscle and rupturing the deep epigastric vessels, and the end came to rest beneath the skin of the abdominal wall. The rung broke off flush with the skin of the buttock. Catheterization revealed no blood in the urine, and rectal examination suggested that the stick had traveled outside the bowel unless possibly just at the anus; therefore, after preliminary treatment for shock, a laparotomy was done, disclosing a large retroperitoneal hematoma from the deep epigastric vessels, but no evidence of intraperitoneal injury. With these facts established it was then a relatively simple matter, after closure of the abdomen, to withdraw the stick from below by combined pressure from above, and the patient made a fairly uneventful recovery, although one small splinter, which could not be detected at the first operation, had to be removed at a later date from a persistently draining sinus beside the rectum.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 36101

PRESENTATION OF CASE

A forty-nine-year-old police captain was admitted to the hospital because of abdominal pain.

Four and a half months before admission the patient experienced the sudden onset of left-sided abdominal pain that was sharp, crampy, nonradiating and associated with nausea but not with vomiting. The pain was not related to meals but was somewhat relieved by food. There was no diarrhea, constipation or tarry stools. Four months before admission the pain became epigastric, occurred three or four hours after meals and was relieved by sodium bicarbonate or milk. Gastric x-ray films were normal, and a barium enema showed diverticulosis. The symptoms improved rapidly on a regimen of Amphojel and milk. Two weeks before admission there was a sudden recurrence of severe, crampy, sharp pain in the left upper quadrant of the abdomen, which was partially relieved by Amphojel. This was most marked three or four hours after meals. Another x-ray examination was reported as showing a duodenal ulcer. The pain continued in spite of milk and Amphojel and was especially severe at night. A few days preceding admission the white-cell count was elevated, and the temperature was 99.8°F.

On physical examination the heart and lungs were normal. There was moderate tenderness to palpation beneath the xiphoid and also on the left side in the anterior axillary line just beneath the costal margin.

The temperature was normal, the pulse was 120, and the respirations were 30. The blood pressure was 190 systolic, 120 diastolic.

Examination of the blood revealed a hemoglobin of 15.8 gm. and a white-cell count of 15,700, with 78 per cent neutrophils. The prothrombin time was 18 seconds (normal, 16 seconds). The urine was normal. X-ray examination after a barium meal was reported as follows:

> The duodenal bulb is markedly deformed and projecting from its superior margin there is a cavity, 5 by 3 cm., that fills with barium and readily empties. The mucosal folds of the duodenum are markedly swollen. There is swelling of the folds of the prepyloric region of the stomach and a suggestion of extrinsic pressure on both the proximal duodenum and the prepyloric region of the stomach.

On the evening of the third hospital day the patient experienced severe, sudden, abdominal pain. A large perforation in the duodenum was sutured. It was believed that a previously walled-off perforation had reperforated. Five days postoperatively a stool containing grossly red blood was passed. On the following day he vomited and passed large quantities of blood by rectum and went into shock. He was treated by transfusion, and the next morning was fully recovered from shock. The nonprotein nitrogen was 82 mg., and the total protein 4.5 gm. per 100 cc., and the chloride 90 milliequiv. per liter. The prothrombin time was 20 seconds (normal, 16 seconds). The stitches were removed on the twelfth postoperative day, and on that evening the wound dehisced. This was resutured. Two days after this operation the patient again vomited blood and went into shock. A transfusion was given, and the first stage of a two-stage subtotal gastrectomy was done. A double jejunostomy was also done. The hemoglobin after this procedure was 10.9 gm. The prothrombin time was 21 seconds (normal, 16 seconds); the total protein was 5.8 gm., and the nonprotein nitrogen 36 mg. per 100 cc., and the chloride 84 milliequiv. per liter. On the eleventh day after this first stage procedure, the patient felt weak and perspired freely. On the following day a stool was black and gave a ++++ guaiac reaction. The hemoglobin was 9 gm. On the fifteenth, seventeenth and twenty-first postoperative days he passed large amounts of blood by rectum, went into shock each time and was brought out each time by transfusions. The hemoglobin had fallen to 4.9 gm. It was decided that this conservative type of treatment had failed, and after suitable transfusions the second stage of the gastrectomy was done. It was possible to remove a large duodenal ulcer with a visible open artery in its base. Postoperatively the patient's condition was good, and the hemoglobin was 10.7 gm. Eighteen days after the gastric resection he vomited about 200 cc. of blood and gastric contents and experienced momentary weakness. The hemoglobin was found to be 7.4 gm. Six days later he went into severe shock and passed large amounts of tarry stools. He was again transfused and started on a constant drip, by stomach tube, of milk and lime water every hour alternated with 1000 units of thrombin. Four days later, in the evening, the patient felt and looked well and there were no untoward signs except a fall of 15 points below his usual systolic blood pressure.

The next morning he complained of severe, epigastric pain. Thirty minutes later he vomited an emesis basin full of blood and again went into a profound state of shock. A blood transfusion administered under pressure was given. Six hours later he had recovered from his profound shock. The abdomen was distended, and peristalsis was absent.

Another operation was performed.

Differential Diagnosis

Dr. G. Gavin Miller*: It is a great pleasure to discuss the differential diagnosis of this interesting case before the Clinicopathological Conference of the Massachusetts General Hospital.

We have before us a case of perforated, and later bleeding, ulcer that persisted in spite of what we would consider adequate surgery. Up to the commencement of the present illness, no mention was made of any previous bleeding or blood dyscrasia. This is an unusual case, and something that was the primary cause of bleeding may have been overlooked. Bleeding may occur from any portion of the upper gastrointestinal tract, from an unsuspected lesion, from diseases of the liver or spleen or from such drugs as Dicumarol and aspirin. At times hematemesis occurs in Bright's disease, infectious fevers and other conditions. However on admission the patient was thoroughly examined and a duodenal ulcer, which had probably been the seat of a previous perforation, was demonstrated. On the third day in the hospital the ulcer reperforated and was sutured. I think it is important to notice that this closure was made in the presence of a former perforation, and therefore probably in the presence of a secondary infection. This may have been the cause of all his later difficulties. Five days later, he commenced to bleed, both vomiting blood and passing blood by rectum. Restored by transfusions, the blood showed a rise in the nonprotein nitrogen, which could be expected after such a massive hemorrhage. The total protein was low, which, with the low-grade infection expected after the suture of a secondary perforation, led to dehiscence of the wound. Repeated hemorrhages necessitated a two-stage gastrectomy, the second stage being carried out because of repeated hemorrhage after completion of the first stage. The duodenal ulcer, with the bleeding vessel demonstrated, was removed.

Maintenance of nutrition had been possible by a double jejunostomy, but in view of the low hemoglobin, the increased prothrombin time and the low total protein, it was obviously difficult to maintain nutrition because of the repeated hemorrhages. However, the patient did well for eighteen days, when gastrointestinal hemorrhage recurred.

This case reminds me of 2 cases recently seen. The first was a case of repeated hemorrhage following removal of a gall bladder and drainage of the common duct. The patient bled both from the T-tube and into the gastrointestinal tract. This man's wound also dehisced, was resutured and remained healed. In spite of forty-eight transfusions he died, and autopsy failed to show the cause of the hemorrhage. Nutrition was not maintained well because of the continuous bleeding, but the original bleeding was not due to malnutrition. In the second case, a subtotal resection was carried out on a patient with a diagnosis of bleeding duodenal ulcer. Following operation, he did well for ten days and then had a massive hematemesis and died. The only cause of bleeding that could be found at autopsy was a small bronchial carcinoma about the size of a pea. These cases show the difficulty of being sure just where the bleeding may be coming from.

In the case under discussion, there was no bleeding for eighteen days after removal of the duodenal ulcer, and then bleeding recurred. Finally, following recovery from severe shock, the abdomen became distended and silent, suggesting peritonitis, and a final operation was necessitated. If he had had peritonitis, it would have suggested another perforation. Bleeding alone might be due to gastrostaxis or to some form of hemorrhagic gastritis, but I have not seen this happen following subtotal resection. In these cases no gross lesion is found in the stomach though the pathologists think they can occasionally demonstrate a recent thrombosis in a small perforated arteriole microscopically.

I am forced to the conclusion in this case that this man had a reperforation and that the first closure was done in the presence of infection. This led to inflammation and persistence of the ulcer, with erosion of a vessel and repeated hemorrhage. The low-grade infection and the debilitation produced by the repeated hemorrhage caused the wound to dehisce. Probably, there was also some infection about the stoma, leading to erosion, hemorrhage and finally perforation. However, such leaks, in my experience, rarely occur after the tenth day, especially when the infection is sufficiently severe to cause such marked secondary hemorrhage. In all our experience, we have never seen a duodenal ulcer fail to heal following adequate gastric resection including removal of the pylorus. Since nutrition was fairly well controlled through a double jejunostomy, it is most unlikely that this bleeding came from an acute gastric lesion due to malnutrition. However, if it was not due to a stomal ulcer or to an acute ulcer it must have been similar to one of the cases described above, when only autopsy will show the cause.

The record states that the patient had diverticulosis, but hematemesis never comes from this source. The record mentions the high nonprotein nitrogen, and one can get hemorrhage in Bright's disease and uremia, but I consider the present rise as being due to repeated hemorrhage.

*Professor of surgery, McGill University Faculty of Medicine, Montreal.

I therefore conclude that this last episode of bleeding came from a new stomal ulcer, and the final picture before the final operation suggests it had perforated.

Dr. Arthur W. Allen: I am sorry that it was left out of the record but this patient had received 200 mg. of Dicumarol on the second postoperative day and another 200 on the third postoperative day after the closure of the perforation. The first massive hemorrhage took place on the fifth day postoperatively. The prothrombin time did disturb us a great deal. It got as high as 40 seconds (normal, 16 seconds), or 10 per cent of normal, which is certainly a dangerous level. The first thought we had, of course, was that the bleeding was associated with the Dicumarol. He responded very quickly to huge doses of synthetic vitamin K and blood transfusions, and the prothrombin time stayed throughout the rest of the period in the hospital within a range of normal. The bleeding was shown to arise actually from the erosion of the gastroduodenal artery that traversed the bed of the ulcer. There was no question about that, because it was found that way by Dr. Welch when he finally operated on this patient. It also accounted for the bleeding prior to the removal of the distal segment of the stomach and the first portion of the duodenum with the ulcer. The fact that the elimination of the gastric contents from the region of the ulcer by the so-called two-stage procedure — that is, cutting through the pylorus and turning it in, and doing a subtotal gastrectomy with anastomosis — failed to stop him from bleeding is in accordance with our previous experience. We had not believed that the procedure would be effective. We have found no way to prevent these people from continuous or repeated hemorrhages other than to interrupt the vessel that is bleeding. The patient that will stop bleeding following any palliative procedure, whether medical or surgical treatment, I believe will stop bleeding just as well without having the gastric juices and so forth diverted from the ulcer bed. We have a good deal of evidence to support that opinion. The amazing thing to us is that this patient could possibly have survived the surgery that he had. When his perforation was first closed the ulcer was found in the worst possible position to get at that one can imagine. There was definite evidence of perforation, which had occurred a few days before. One could tell that by the character of the material that we removed from the abdominal cavity, and we did not believe that this ulcer was resectable at the time we closed the perforation. Dr. Welch proved later that it was resectable and in two stages did so.

The final episode is something that is of great interest to us too. We were probably wrong about the assumption that the Dicumarol had any effect on the first bleeding. However, we blamed it on that until we saw the condition of the ulcer and the eroded vessel.

Dr. Claude E. Welch: He was a very sick man. Every time we operated on him we had our backs to the wall. I have to make some apologies for the surgery we had to do. But at the time of the second operation — that is the first-stage gastrectomy — when I opened the abdomen it actually took fifteen minutes to identify the stomach in the presence of the peritonitis. The first-stage gastrectomy was not, therefore, what we call an adequate first stage. It consisted of division of the stomach somewhere between the junction of the lower third and the midportion. I thought I would kill the patient if I did more. There was enough peritonitis so that I had to drain the lesser omental bursa, and the drain came out rather close to the suture line. The second-stage gastrectomy was just as described. I was happy that this bleeding vessel had been discovered. There was a clot in it at the time we opened it. The gastroduodenal artery had been eroded 1 cm. before its origin from the hepatic artery. We were greatly disappointed that he started to bleed again. We considered the diagnosis of stomal ulcer versus gastritis. The terminal episode we thought probably represented perforation of a stomal ulcer with pneumoperitoneum. The last operation was an ante-mortem autopsy. The patient was nearly moribund, but we thought a pneumoperitoneum might be relieved. He had tremendous ileus of the stomach and intestine instead. It was impossible to do anything, and he died shortly afterward.

Clinical Diagnoses

Duodenal ulcer, with perforation and peritonitis.
Massive gastrointestinal bleeding.

Dr. Miller's Diagnosis

Bleeding perforated stomal ulcer.

Anatomical Diagnoses

Massive bleeding from gastrojejunal (stomal) ulcer eighteen days after gastric resection for duodenal ulcer.

Perforation of stomal ulcer with localized peritonitis.

Pathological Discussion

Dr. Benjamin Castleman: I can well understand the difficulty Dr. Welch had at operation because at autopsy there was marked ileus and many adhesions. After dissecting away all the adhesions, we found some evidence of acute inflammation in the region of the anastomosis. This region was adherent to the undersurface of the ulcer, and as it was separated from the liver a small hole, about 5 mm. in diameter, was apparent. I believe this had been sealed off, however, by the inferior surface of the liver, but there might have been at one time a little seepage through it. On opening the stomach and jejunum we found near the anastomosis on the

jejunal side a deep crater measuring about 1 cm. in diameter and about 0.5 cm. in depth, at the bottom of which was this little hole that had been adherent to the liver. In the center of this crater was a pouting vessel that apparently was the source of the bleeding. We have here, then, an example of stomal ulcer occurring within a very short period following anastomosis — eighteen days. Microscopical examination of the stomach slide showed plenty of acid-secreting cells. The ulcer was definitely peptic in nature rather than one due to infection.

DR. MILLER: I do not know that there is any further comment except that it is interesting that the stomal ulcer should have occurred so soon after resection. We now know because of the discussion that the resection was not adequate. It is interesting to me how much major surgery patients with peritonitis will stand. I suspect that all the infection and peritonitis played a part in the rapid onset, with further ulceration, bleeding and finally death.

DR. ALLEN: I do not believe I know of one occurring in eighteen days.

DR. EDWARD B. BENEDICT: Why are there not more following this procedure? We are doing it commonly now.

DR. ALLEN: There have been two or three, but usually the second operation takes place within six weeks of the first and that difficulty is avoided. Of course, patients who have had higher resections than this improve.

DR. CASTLEMAN: Some years ago Hurst and Stewart* reported a series of 131 autopsy cases of duodenal ulcer in patients who had had gastric resection. One third of these patients died within ten days of the operation, and the authors found no jejunal ulcers. Another third died between ten days and two months postoperatively, and only 3 out of 41 in that group had jejunal ulcers. Of the third group who died after two months, 22, or about half, had jejunal ulcers. Our case would fit in with their second group, in which the incidence of jejunal ulcer is very low.

*Hurst, A. F., and Stewart, M. J. Jejunal and gastrojejunal ulcers. *Lancet* 2:742-748 and 805-809, 1928.

CASE 36102

PRESENTATION OF CASE

A fifty-three-year-old Italian-born cook was admitted to the hospital complaining of abdominal distention and pain.

Five weeks before admission, after previous good health, he began to lose his appetite. A few days later he noted that his urine was very dark. Four weeks before admission moderately severe, gripping pain appeared, starting in the right upper quadrant and radiating across the abdomen to the left side without involving the lower abdomen, chest or back. There was no nausea, vomiting, constipation or diarrhea. The patient stopped work, and consulted a physician, who noted jaundice of the scleras and skin. A low-fat diet and rest were prescribed. The pain and dark urine persisted, and three and a half weeks before entrance to the hospital acholic stools were noted. They subsequently ranged from normal to clay color. They were never black or blood stained. Three weeks before admission the abdomen began to increase in size, and that continued up to the time of admission. There had been no itching, chills, fever or pain related to meals. The patient lost 15 pounds in the six weeks before admission.

Twenty-five years previously an uncomplicated appendectomy for acute appendicitis was performed. Twenty years before admission he had a two-week episode of painless jaundice, loss of appetite and dark urine for which he rested at home.

Physical examination showed a jaundiced, afebrile man in no acute distress. Over the right chest at the base posteriorly there were dullness, decreased breath sounds, decreased tactile fremitus and coarse inspiratory rales. The heart was normal. The abdomen was tense and protuberant, and signs of fluid were present. The liver edge extended 3 fingerbreadths below the costal margin and was slightly tender to deep palpation. The spleen was not palpable, and no masses were felt.

The pulse was 78, and the respirations 20. The blood pressure was 135 systolic, 85 diastolic.

Examination of the blood showed a white-cell count of 5800, with 75 per cent neutrophils, 24 per cent lymphocytes and 1 per cent monocytes. The urine was dark brown, with a +++ test for bile and a urobilinogen of 3.5 Ehrlich units. There was no albumin or sugar. The sediment was normal, and the specific gravity 1.025. The stools were brown, semiformed, guaiac negative and positive for urobilin and urobilinogen. Chemical examination of the blood serum demonstrated an alkaline phosphatase of 10.8 units per 100 cc.; the prothrombin time was 19 seconds (control, 18 seconds), and the fasting blood sugar 105 mg., the nonprotein nitrogen 26 mg., the albumin 3.75 gm., the globulin 3.64 gm., the cholesterol 390 mg., and the cholesterol esters 188 mg. per 100 cc. The van den Bergh reaction was 4 mg. per 100 cc. direct and 6.0 mg. total, and the cephalin-flocculation test was + in twenty-four and forty-eight hours. The bromsulfalein test revealed 46 per cent retention of the dye after forty-five minutes. X-ray studies showed both leaves of the diaphragm to be high, and there were plate-like foci of atelectasis in both lower lobes. A film of the abdomen disclosed a normal-sized spleen, liver enlargement and abdominal fluid. A urogram demonstrated some lobulation of the lateral border of the left kidney, and the middle calyx was filled in this region, but the infundibulum never filled out completely. The right kidney was normal. A gastrointestinal series showed esophag-

eal varices, and varices in the greater curvature of the stomach. The stomach was otherwise normal. A peritoneal tap produced 750 cc. of bile-stained, cloudy fluid with a specific gravity of 1.010, a white-cell count of 3000 and a red-cell count of 45,000 per cubic millimeter. The fluid was sterile and negative for tumor cells.

The patient remained afebrile and was discharged on the twelfth hospital day. At home he remained comfortable, but apprehensive. An abdominal tap produced 3 liters of fluid, but it rapidly reaccumulated. One week after discharge there was a small hematemesis. Two weeks after discharge, and nine weeks after the onset of his illness, he had a massive hematemesis, with shock, and died in a few hours.

Differential Diagnosis

Dr. Myles P. Baker*: The story is that of a middle-aged Italian who came into the hospital because of four weeks of painful jaundice — pain that was upper abdominal in location, perhaps more on the right side than on the left. For three weeks he had had abdominal swelling and was shown on admission to be jaundiced and to have ascites and signs at the lung bases consistent with a high diaphragm in association with the accumulation of a fair amount of ascitic fluid. The liver was large and slightly tender.

With these findings the physician who saw him first would, I suppose, consider the possibility of infectious hepatitis only with a good many doubts. The relative well-being in the presence of ascites is important. I suspect that if the patient had had infectious hepatitis with ascites he would have been a good deal sicker than he apparently appeared. Moreover, he had no fever.

The laboratory tests, particularly those of liver function, were not too decisive diagnostically. There was evidence of liver-cell damage, for the patient had an elevated bilirubin, an excess of urobilinogen in the urine (the high normal is 1.2 Ehrlich units) and a decrease of serum albumin and increase in serum globulin levels. The last finding is what one sees in liver disease of some weeks' standing. One notes with surprise that the cephalin-flocculation test was normal, something that certainly would be unusual if he had a diffuse liver infection. Elevation of the serum cholesterol is something that one is familiar with in the presence of liver disease of some duration. It would be unusual to find this in a man who had been ill for only five weeks, but it is interesting that the level of cholesterol esters, about 50 per cent, was not significantly lowered. One could interpret that as being evidence of the absence of acute hepatitis. The level of bilirubin in the blood was not particularly high considering the amount of scleral and skin jaundice noted. The figure of 46 per cent bromsulfalein retention is a little hard to draw many conclusions from in the presence of jaundice. This test is not usually done in the presence of jaundice because we know it is going to show some retention. One might wonder, however, if a figure of 46 per cent is not disproportionately high. Retention to this degree in a liver in which the disease has led to a bilirubin level of only 6 mg. per 100 cc. in the blood would suggest a liver disease of longer standing than the four or five weeks for which this man had had symptoms. The normal prothrombin time, the negative cephalin-flocculation test and the low normal percentage of cholesterol esters are findings that one sees in early extrahepatic obstruction or common-bile-duct obstruction. But after all, in this man, we are dealing with an illness that had been going on for four or five weeks, and by that time I would expect more definite evidence of liver-cell damage than these tests indicated.

Such information as we can derive from these liver-function tests is entirely compatible with a diagnosis of portal cirrhosis — particularly the interchange of the serum albumin and globulin, the elevated urobilinogen and the rather marked bromsulfalein retention without very definite evidence of liver-cell damage as could be judged from a positive flocculation test. The critical finding here is, of course, that of esophageal varices, and to check on that we had better ask Dr. Hanelin to show us the x-ray films.

Dr. Joseph J. Hanelin: I have only a postero-anterior chest film; the lateral film is not available. The diaphragm is elevated. The linear markings in the lungs are prominent, probably as a result of elevation of the diaphragm. There may be a few linear areas of atelectasis at the bases. Films of the esophagus demonstrate the presence of varices. There was a large irregular defect along the greater curvature of the stomach, which was considered to be due to varices also, but definitely to exclude the presence of neoplasm here a balloon was inserted into the stomach, which was then distended with air. This showed the fundus to be flexible; the defect was obliterated by pressure from the balloon. Both liver and spleen appear to be somewhat enlarged. The kidneys are grossly normal in outline. There is slight lobulation of the left kidney, but this is extremely minimal and only of questionable importance.

Dr. Baker: The presence of esophageal varices, to me, limits the diagnosis to such processes as can cause portal hypertension with the development of a collateral circulation involving the coronary vein and leading to varices at the lower end of the esophagus. Cirrhosis of the liver is by all odds the commonest cause of portal hypertension and the development of esophageal varices. Occasionally, there is a rare case of portal-vein thrombosis, usually involving the splenic vein as well, as a result of which esophageal varices develop and in which studies do not reveal any intrahepatic cirrhosis. I do not see that we have any evidence for such a process here. The initial symptoms that this man had —

*Associate physician, Massachusetts General Hospital.

namely, loss of appetite, pain and swelling of the abdomen — are the characteristic symptoms signaling the decompensation of a cirrhotic liver. Jaundice occurs mildly in something less than 10 per cent of such cases; there is abdominal swelling initially in 25 per cent; pain was the initial symptom in 10 to 15 per cent of cases of cirrhosis of the liver studied in the Welfare Hospital* in New York City — a rather higher figure than I had ordinarily associated with portal cirrhosis as an initial symptom. There is nothing in the story, therefore, that seems to me out of keeping with a diagnosis of portal cirrhosis. This man died two months after the onset of his first symptoms, but that does happen. In fact, a fatal hematemesis may be the first indication of an underlying process that has been asymptomatic up to that time.

What other possibilities could be diagnostically important in this case? Is there any evidence of a primary hepatoma or cholangioma of the liver, since these patients frequently have a portal cirrhosis in their background? Primary cancer of the liver characteristically begins insidiously as this man's trouble did and proceeds rather rapidly to a fatal outcome. Pain is common, and this man had a good deal of pain. It is said that this, in association with a large liver and ascites, should make us think of a primary cancer of the liver. Bloody ascitic fluid should make us think of a primary cancer of the liver. This man's ascitic fluid was not grossly bloody. There is no x-ray evidence that is absolutely decisive for the presence of primary cancer of the liver unless one can demonstrate more elevation of the right leaf of the diaphragm than this man had, indicating tumor in the right lobe of the liver working upward. If one can demonstrate such a lesion in the liver by x-ray examination, one is surer of one's ground. It seems to me here that although it is a possibility, we have no data that make it more than just that — more than a possibility.

Was this man's rapid progress to a fatal issue dependent on the development of portal-vein thrombosis? That is a rather uncommon (3 per cent) complication of portal cirrhosis, which leads to rapidly accumulating ascites such as this man proved to have, but it is very difficult to diagnose before death. It is something that one suspects in the presence of rapid decompensation, but the symptoms referable to it are those of the much more common situation — a completely decompensated cirrhosis of the liver.

My diagnosis here, then, is portal cirrhosis of the liver with esophageal varices and fatal hemorrhage either from the esophageal varices or from dilated veins in the upper end of the stomach.

Dr. Gerardo M. Balboni: I had the advantage of having seen the patient about a month after he was taken ill. He had consulted his lodge doctor for an attack of upper abdominal pain from which he recovered sufficiently in a few days to return to work. A week later he again consulted this doctor for epigastric distress. The physician reported that he was then slightly jaundiced, and had x-ray studies done. I saw the patient a month after the x-ray studies were done. At that time there was marked jaundice, some evidence of fluid in the abdomen, a spleen that could not be felt and a markedly palpable liver, which I thought was neoplastic. The x-ray studies were negative except for esophageal varices. The inability to demonstrate a primary lesion elsewhere, and the short duration of the symptoms, the progressive weakness, the epigastric distress, the large liver, ascites and jaundice made me believe that he had a primary cancer of the liver for which he was hospitalized.

A Physician: Could this have been Mediterranean anemia?

Dr. Chester M. Jones: Not without a spleen that is easily noted. I saw a large number of such patients in Greece, and all of them had very large spleens. If the liver was involved that was a minor rather than a major affair, and in those cases the spleen was very obvious.

A word about the laboratory tests: it seems to me that if there is only portal cirrhosis of the liver, it is very unusual to have a negative cephalin-flocculation test in association with marked retention of bromsulfalein, an elevated phosphatase and moderate hyperbilirubinemia. Furthermore, the cholesterol was higher than one would expect with portal cirrhosis of the liver. It seems much more likely to go with some form of intrahepatic or extrahepatic obstruction to the flow of bile.

Dr. Daniel S. Ellis: Do you think you can explain this picture, including the varices, by cancer alone?

Dr. Jones: We have had such cases. I recall a case of cancer of the rectosigmoid in which the liver was filled with metastatic cancer. That patient developed varices and had a fatal hemorrhage from them. Of course, it is unusual, but I am sure it does occur.

Dr. Ellis: I was asked to see this patient with regard to doing a liver biopsy. He had a diffusely enlarged liver, and, as I remember it, I thought the primary disease was portal cirrhosis and that he probably had a hepatoma superimposed. The biopsy was done transthoracically, for he had a good deal of ascites and it seemed easier to go through the thorax than through the abdomen. Dr. French did the biopsy, and at the time of biopsy there was no tissue that could be defined as normal hepatic tissue.

Dr. Jones: May I make one more point, Dr. Castleman? I think that Dr. Balboni noticed initially that there was only moderate enlargement of the liver, which enlarged very rapidly from then on. It is an important point.

*Ratnoff, O. D., and Patek, A. J., Jr. Natural history of Laennec's cirrhosis of liver: analysis of 386 cases. *Medicine* **21**:207-268, 1942.

DR. BAKER: I think that is very important. It would be hard to explain the rapid enlargement of the liver on the basis of the usual cirrhosis of the liver.

CLINICAL DIAGNOSIS

Primary liver-cell carcinoma?

DR. BAKER'S DIAGNOSIS

Portal cirrhosis of liver, with hematemesis from esophageal varices.

ANATOMICAL DIAGNOSES

Hepatoma, diffuse, multicentric in origin.
Cirrhosis of liver, postnecrotic type.
Massive hemorrhage from esophageal varices.
Thrombosis of portal vein.
Ascites.
Jaundice.
Pulmonary edema and congestion.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: This is a photomicrograph of the biopsy (Fig. 1). Here there are

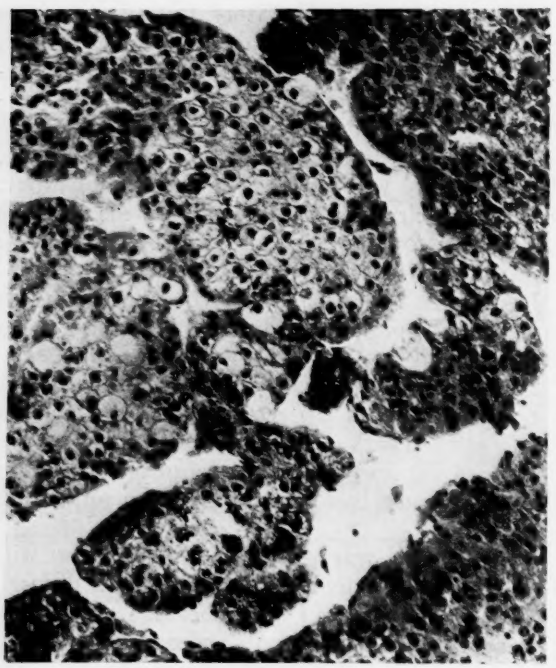

FIGURE 1.

large polyhedral clear cells, some with mitoses. Some of the cells are not so clear and some are very large, but none look like normal liver cells. This was obviously carcinoma, but we were not too sure whether this was a primary liver-cell carcinoma or a metastatic carcinoma. Dr. Mallory leaned toward a primary tumor of the liver because he recalled seeing clear cells like these in a previous case. I remember seeing one case like this that turned out to be a primary cancer of the stomach, and when the first gastrointestinal series showed a gastric defect, I believed that it was a metastasis from carcinoma of the stomach. Another point that arose was that there was a slight defect in the kidney, and perhaps these clear cells were from a hypernephroma.

At autopsy the entire parenchyma of the liver was replaced by nodules 3 to 10 mm. in diameter. Some were hard, and others were soft; some were green, and others were yellow or orange. At the time of autopsy we were not sure whether this was a primary hepatoma or whether it was just portal cirrhosis of the liver with varying types of regeneration. However, since the biopsy had been definitely carcinoma we decided that some of the nodules represented hepatoma, and this was confirmed microscopically. Many of the islands of tumor looked like mature liver cells and were secreting bile. These foci represented a much more differentiated form of primary liver carcinoma than other areas that had the clear cells — such as were seen in the biopsy. In addition, throughout all sections one could make out very definite evidence of islands of regeneration of normal liver cells such as one sees in portal cirrhosis. This patient, therefore, had underlying the tumor an old atrophic type of portal cirrhosis, and perhaps the jaundice twenty years before was associated with the initial factor in the production of the cirrhosis. We found varices of the esophagus and stomach, and in a few places in the esophagus there were some erosions — apparently the site of the terminal hemorrhage.

DR. BAKER: He was a man who died of a complication of cirrhosis of the liver, who happened to have a small hepatoma?

DR. CASTLEMAN: It was not small. The hepatoma involved about two thirds of the liver. It was almost certainly multicentric in origin, rather than originating in one spot and metastasizing throughout the liver. I still cannot understand the clinical tests because, anatomically, it does not look as if he had very much liver tissue that was working.

DR. BAKER: Did he have any metastases?

DR. CASTLEMAN: No.

DR. BAKER: Do you think the tumor could have produced the collateral circulation?

DR. CASTLEMAN: There was enough cirrhosis to account for the varices, but the tumor probably added to the portal hypertension. The portal vein, as well as many of its branches, was filled with tumor thrombi.

DR. ELLIS: Was the kidney normal?

DR. CASTLEMAN: Yes, he had normal kidneys.

DR. JONES: This is a good example of the impossibility of making a diagnosis wholly on the basis of laboratory tests. In this particular case it seems to me to be a very good argument for early biopsy of the liver, to get an exact picture of what is going on.

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QUALITY OF MEDICAL CARE

McCombs, elsewhere in this issue of the *Journal*, gives a list of the factors that, according to his judgment, are impairing the efficiency of physicians in their efforts to deliver good medical care. The importance of all these factors can be admitted, provided they are not accepted with equanimity.

They are, in general, ineffective or obsolete methods of practice established by tradition, lack of continuing educational opportunities for practicing physicians, the competitive nature of medical practice and the ignorance of laymen regarding health, disease and methods of treatment. To these must be added the black medicine of all times — unethical activities and frank malpractice.

The author goes into detail in explaining how the necessity for making a living or the desire to make a particularly good living contributes to these imperfections in the practice of a profession that should be as nearly perfect as possible. The fixed fee for services rendered is considered by McCombs a basic evil; so are the sloppy methods that may result from large practices; so is the fixed idea (forced on the profession by the majority of its patients) that some form of treatment must be given.

Devious methods are employed by a certain class of physicians to circumvent the fixed idea of the fixed fee; among these are the unfortunate but far from universal practice of using diagnostic procedures that these doctors are not qualified to carry out or interpret, and the attempting of therapeutic procedures, particularly in surgery, that are beyond their capabilities. The private hospital is a constant temptation to sharp practice and over-keen competition because of the necessity of supporting it. The disparity of fee schedules between general practitioners and specialists and between internists and surgeons has been a temptation drawing unqualified practitioners into specialization.

The medical profession is aware of the inadequacies and the faults that are apparent in its ministrations, and it is not proud of them. It knows that improved medical care should follow their abatement, and it has been working steadily, if not as yet with sufficient vigor, in that direction. The art is long and experiment difficult, yet one has but to view the advances of a half century to see how much progress has been made, not only in the science but in the temperate regulation of medical practice.

Since the establishment of the College of Physicians at the instance of Thomas Linacre near the end of the fifteenth century, the profession has sought to monitor itself and to improve its services. This it has been doing, with increasing scope and effect through its academies, its colleges, its societies and its associations; through professionally inspired boards of registration and departments of health and through codes of ethics and specialty boards; through postgraduate courses in ever greater numbers, and by careful attention to standards of training and of hospital administration, as have been fostered by such agencies as the Council on Education and Hospitals of the American Medical Association, the American College of Surgeons and,

locally, the New England Surgical Society. The public, moreover, is being increasingly better informed of what is right and wrong in medical practice. There is much left to be done, but it must be accepted, on faith if necessary, that a learned professional group, composed largely of men and women of good will, can, in the long run, most conservatively and effectively regulate its own efforts from within.

PENICILLIN-RESISTANT STAPHYLOCOCCI

THE original discovery of penicillin by Fleming[1] was based on the chance observation of its lytic activity on staphylococcal colonies. When this antibiotic was later prepared in a therapeutically useful and potent form it was expected to be the long-sought answer to the problem of staphylococcal infections. The experience of the last few years, however, has revealed that a significant proportion of such infections are due to strains that are of high resistance to penicillin in vitro and are clinically resistant to treatment even with large doses of this antibiotic. The paper by Beigelman and Rantz in this issue of the *Journal* presents evidence of this point that is now probably familiar to most physicians, especially those with much hospital experience.

The origin of these penicillin-resistant strains of staphylococci is a matter of considerable interest. There is little doubt that penicillin is used very widely, and in many hospitals it is used almost routinely both for therapy and for prophylaxis in diverse conditions, most of them not in the least concerned with penicillin-susceptible bacterial infections. It is reasonable to expect that such widespread use of this agent should tend to eliminate penicillin-sensitive strains and leave the resistant ones to spread. Similar situations have been encountered in treatment with the sulfonamides. A case in point was the spread of infections with sulfonamide-resistant streptococci following the universal use of sulfadiazine prophylaxis in certain military units in attempts to reduce the incidence of respiratory infections.[2,3] The almost complete elimination of sulfonamide-susceptible gonococci after the universal use of these drugs in prophylaxis and treatment of gonorrhea is another example in point.[4] A marked increase in sulfonamide-resistant gonococci was also encountered in groups subjected to mass sulfonamide prophylaxis of respiratory diseases.[5]

There is also a certain amount of direct evidence tending to support the view that the extensive use of penicillin has resulted in an increase in the proportion of penicillin-resistant staphylococci. In St. Mary's Hospital, where Fleming carried out his important researches, a progressive increase in the proportion of resistant strains of pathogenic staphylococci isolated in three successive periods was observed: 14 per cent of the strains of pathogenic staphylococci isolated from April to November, 1946, were resistant; in the period from February to June, 1947, 37 per cent were resistant and between February and June, 1948, 59 per cent of the strains of staphylococci were found to be resistant.[6]

More recently Forbes[7] found only 5 penicillin-resistant strains among 40 strains of staphylococci (12.5 per cent) that were isolated from as many outpatients in whom contact with hospital patients or with penicillin could reasonably be ruled out. By way of contrast 26 penicillin-resistant strains, or 68 per cent, were found among 38 cultures of staphylococci that were isolated from patients whose infections had arisen in the hospital, where, of course, penicillin was being used very widely. However, when Forbes studied the source of penicillin-resistant strains among his hospitalized patients, he found that 25, or 59 per cent, had been recovered from 41 patients who had previously received penicillin; among the patients who had not received any penicillin treatment prior to the time of isolation of the organisms, 25, or 43 per cent, of 51 strains of staphylococci were found to be resistant. The latter proportion, though apparently smaller, is impressive and suggests that the mere administration of penicillin prior to the isolation of a strain is not necessarily the only or even the primary factor in determining the resistance of the strains isolated from hospitalized patients.

Such data suggest either that penicillin treatment has only a relatively slight effect, if any, on the resistance of strains isolated or that patients

who have not previously been treated had acquired their resistant strains from treated patients. This might have occurred either directly or indirectly, as Forbes believes, by way of hospital personnel who carried such resistant strains in the nose or on the skin and who in turn acquired them from treated patients.

It is of interest, however, that occasional resistant strains were encountered as early as 1942,[8] and an appreciable number were found before 1945, when penicillin first became available in quantities large enough to be used extensively.[9-11] Furthermore, in the data presented by Beigelman and Rantz, there seems to have been a rather sudden and significant increase in the proportion of resistant strains from their hospitalized patients after 1945, and no further important increase occurred after that time.

The number of cases studied by the Stanford workers was small, but similar results have been obtained at the Boston City Hospital. In a study soon to be published,[12] it was found that strains isolated at that hospital since the earliest use of penicillin divided themselves quite sharply in their sensitivity and resistance to penicillin into those isolated before 1946 and those obtained during and after that year. Only a small proportion of the former were resistant, whereas about half or more of those isolated since 1946 could be classified as resistant. The time of this change from a low to a high percentage of resistant strains coincides with the end of the war, when large amounts of penicillin became available and when, with the steady reductions in price, the present practice of almost universal use of penicillin for both treatment and prophylaxis became popular. On the other hand, this also corresponds to the time when the changing character of commercial penicillin was recognized.[13] After that time highly purified preparations of penicillin G became essentially the only type of drug that was marketed on any large scale. The possibility cannot, therefore, be ruled out that the earlier preparations contained substances that had greater activity against a wider range of staphylococci than the currently available preparations of crystalline penicillin G.

Be that as it may, it is now clear that penicillin-resistant staphylococci are highly prevalent. Pathogenic strains of such resistant staphylococci are found in people who have never received penicillin, and even in newborn infants.[14] They are more likely to occur in patients who have received continuous therapy with penicillin for various reasons. The most resistant strains are found in persons after treatment with large doses of penicillin given over long periods either for prophylaxis or for therapy. Apparently normal persons may carry in the nose pathogenic strains of staphylococci that are penicillin resistant, and they may transmit infections with these strains to others. Finally, not only are these strains of staphylococci resistant in the test tube, but also infections with such strains resist treatment with large doses of penicillin.

Fortunately, the sensitivity of any strain to penicillin is independent of its sensitivity to other antibiotics. Streptomycin has proved useful in the treatment of some of the infections with penicillin-resistant strains. Bacitracin has also been employed with some success in the local therapy of superficial infections. More recently aureomycin has been found to be much more effective in such infections, and there are now several reports of success with this agent in the treatment of severe and prolonged staphylococcal infections that have resisted treatment with all previous agents.[15, 16] The possibility and indeed the probability exists that, as the use of these more recent agents becomes widespread, increasing numbers of strains of staphylococci will be encountered that will prove resistant to them as well. This should serve as a warning against the indiscriminate administration of such highly important agents, particularly their use over long periods for what is thought to be prophylaxis or whenever there is no real justification for using them.

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EASTER SEAL CAMPAIGN

THE response of Massachusetts citizens to the Easter Seal Campaign of the Bay State Society for the Crippled and Handicapped, which begins today, will demonstrate the willingness with which a free society faces the problem of helping its less fortunate members. The goal of $275,000 seems relatively modest when compared with the sums asked in other philanthropic drives, and it should be remembered that the program to help handicapped children and adults does not duplicate the work of any other agency. In terms of humanitarian aid to the unfortunate, the work of the Society is both necessary and extremely praiseworthy: support for centers for treatment and training for children with cerebral palsy; a program for the control of epilepsy; and rehabilitation and new hope for men, women and children who would otherwise find no relief from their distress.

It is to be hoped that the generous contribution of the people of the Commonwealth will allow the Society to collect its quota and continue its financial and spiritual aid to the crippled and handicapped.

SHORTAGE OF PUBLIC-HEALTH PHYSICIANS

THE supply of fully trained personnel to man full-time health units is a cause of grave concern. There appears to be an imminent shortage in some of the categories of health workers desired in these union health departments, especially in trained medical officers. Public health, which depends largely upon publicity and public education for its results, appears so far to have failed to draw attention, at the collegiate premedical level, to the attractiveness and the rewards of public-health services — an important oversight indeed.

Collegiate advisers and the deans of medical schools may well consider the advisability of pointing out to selected and medically inclined students the extreme interest and pleasure inherent in public-health work. Last year the American Board of Preventive Medicine and Public Health was established. It may well be a function of this board also to publicize the opportunities in the field of public health.

One of the homeopathic fraternity is down upon Dr. Hooker, of Norwich, Conn., in consequence of something introduced into his charming work, Physician and Patient. It is strange how testy are some of the young converts to Hahnemannism. Great sinners, says the proverb, make the greatest saints.

Boston M. & S. J., *March 6, 1850*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

FOSTER — Brigadier General George B. Foster, Jr., M.C., U.S.A. (retired), of Cambridge, died on December 31. He was in his sixty-sixth year.

General Foster received his degree from Jefferson Medical College of Philadelphia in 1907. He was medical director of Cambridge City Hospital and former commanding officer of O'Reilly General Hospital, Springfield, Missouri, and was a fellow of the American College of Physicians and the American Medical Association. He served in both world wars, being awarded the Legion of Merit of this country and the Legion of Honor of France.

His widow, a son, two daughters, two sisters and six grandchildren survive.

THOMES — John Blanchard Thomes, M.D., of Pittsfield, died on December 5. He was in his eightieth year.

Dr. Thomes received his degree from Dartmouth Medical School in 1896. He was a member of the staffs of St. Luke's, Hillcrest and Pittsfield General hospitals and a fellow of the American College of Surgeons.

His widow survives.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COURSE FOR SCHOOL PHYSICIANS

The following is an open letter to all school physicians, superintendents and boards of health:

The annual orientation course for school physicians offered by the Massachusetts Department of Public Health and the Harvard School of Public Health, Department of Maternal and Child Health, has received the following tentative calendar.

This is a thoroughly revised course and those who have already attended courses may find it of equal value to them as to those who have not yet attended these courses.

Stipends covering expenses and amounting to $10 per session are again available through Maternal and Child Health funds. They are limited in number, and early registration is therefore advisable.

Since we do not have a complete list of school physicians it is advisable that school superintendents and boards of health assure themselves that their men have received a copy. The Bureau should be advised of such instances in order that our files may be made complete.

PROVISIONAL CALENDAR

April 5. 2–5 p.m. The physical development of children in the age period five–eighteen years. Dr. Harold Stuart (professor of maternal and child health, Harvard School of Public Health) and associates.

April 12. 2–5 p.m. The emotional development of children in the age period five–eighteen years. Dr. Warren T. Vaughan, Jr. (research fellow in mental health, Harvard School of Public Health, psychiatrist, Phillips Exeter Academy and consulting psychiatrist, Newton public schools) and associates.

April 26. 2–5 p.m. The identification of children needing medical care and related services. Dr. Samuel Dooley (assistant professor of pediatrics, Cornell University Medical College, and assistant professor of child health, Harvard School of Public Health) and associates.

May 3. 2–5 p.m. The functioning of school health services to meet the needs of school-age children. Dr. William Schmidt (associate professor of maternal and child health, Harvard School of Public Health) and associates.

May 10. 2–5 p.m. Community and social factors of practical significance in the school health program. Dr. William Schmidt (associate professor of maternal and child health, Harvard School of Public Health) and associates.

This course will be given at the Harvard School of Public Health at 55 Shattuck Street, Boston, Massachusetts.

ALLAN R. CUNNINGHAM, M.D.
Chief, Bureau of Health Information

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Textbook of Neuropathology, with Clinical, Anatomical and Technical Supplements. By Ben W. Lichtenstein, M.S., M.D., associate professor of neurology, University of Illinois College of Medicine, state neuropathologist, Illinois Neuropsychiatric Institute, attending neurologist, Cook County Hospital, professor of neurology, Cook County Graduate School of Medicine, and attending neuropsychiatrist, Mount Sinai Hospital, Chicago. 8°, cloth, 474 pp., with 282 illustrations. Philadelphia: W. B. Saunders Company, 1949. $9.50.

This new textbook has been written primarily for the medical student and for those training in neurology, psychiatry, pathology and neurosurgery. The earlier chapters discuss the pathology of the nervous system in general, followed by chapters on inflammatory diseases, hemorrhage and vascular disorders, hydrops, hyperplasia, tumors, malformations and deformities, adventitious and metabolic substances and muscular disorders and related states. The clinical supplement presents a list of 114 syndromes, paralyses and uncommon diseases. Lists of references are appended to the various chapters. There is a good index, and the type, printing and illustrations are excellent.

Clinical Biochemistry. By Abraham Cantarow, M.D., professor of biochemistry, Jefferson Medical College; and Max Trumper, Ph.D., Commander, H(S), USNR, lecturer in clinical biochemistry and basic science co-ordinator, Naval Medical School, National Naval Medical Center, Bethesda, Maryland. Fourth edition. 8°, cloth, 642 pp., with 38 figures and 22 tables. Philadelphia: W. B. Saunders Company, 1949. $8.00.

This fourth edition of a standard work has been revised and brought up to date since the publication of the third edition in 1945. New material has been added on chemical changes in shock, thymol turbidity and flocculation, fatty liver, the crush syndrome (lower-nephron nephrosis), potassium in the treatment of diabetic coma, alarm reaction, goitrogenic agents and new methods of studying adrenocortical function. The sections on renal and respiratory regulation of the acid-base balance, pigment metabolism in relation to jaundice, carbohydrate, lipid and protein metabolism, thyroid function, adrenal function, absorption and storage of iron, action of parathyroid hormone, renal physiology, vitamins and experimental diabetes have been extensively revised. The material is well organized and well written. Bibliographies are appended to the various chapters. There is a comprehensive index. The publishing is excellent, and the book should be in all medical libraries and available to all persons interested in the subject.

NOTICES

MASSACHUSETTS PHYSICIANS CLUB

A meeting of the Massachusetts Physicians Club will be held at the Hotel Kenmore, Boston, on Tuesday, March 14, at 8:30 p.m.

Dr. William P. Murphy will speak on the subject "Diagnosis and Treatment of Hyperchromic Anemias."

Interested physicians and medical students are invited.

GREATER BOSTON MEDICAL SOCIETY

The March meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on March 16 at 8:15 p.m.

The meeting will consist of a symposium on psychosomatic medicine. Dr. Louis S. Chase will speak on the subject "Mechanisms behind the Common Neuroses." Dr. Henry M. Fox will discuss "Mechanisms Responsible for Specific Psychosomatic Symptoms." And Dr. Alfred O. Ludwig will consider "The Psychologic Aspects of Organic Illness."

SOUTH END MEDICAL CLUB

A luncheon meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, March 21, at 12 noon.

Dr. Robert E. Gross, Ladd Professor of Children's Surgery, Harvard Medical School, and surgeon-in-chief, Children's Hospital, will speak on the subject "Surgery in Infancy."

All physicians are cordially invited to attend.

SOCIETY OF AMERICAN BACTERIOLOGISTS, NORTHEAST BRANCH

A meeting of the Northeast Branch of the Society of American Bacteriologists will be held at Simmons College, 300 The

Fenway, Boston, on March 24. The afternoon session, beginning at 4:00 o'clock will be devoted to original contributions in the field of microbiology. After dinner, Dr. Joseph L. Melnick, of the Department of Preventive Medicine, Yale University School of Medicine, will speak on the subject "The Biology of Poliomyelitis and Related Viruses."

Persons desiring dinner reservations should get in touch with Dr. Genevieve Young, Boston University, 675 Commonwealth Avenue, Boston, before March 20.

HARTFORD MEDICAL SOCIETY

The program of the Hartford Medical Society for the next three meetings is as follows:

Monday, March 20. Dr. Robert Elman, of St. Louis, will present an afternoon clinic on a subject to be announced later and an evening address entitled "Protein, Electrolyte and Water Balance."

Monday, April 3. Dr. James M. Baty, of Boston, will present a clinic on the subject "Office Pediatrics" in the afternoon. His evening address will be entitled "Hemorrhagic Nephritis in Children."

Monday, April 17. Dr. Willard O. Thompson, of Chicago, will present an evening address on the subject "Endocrine Therapy in Daily Practice."

PHILADELPHIA COUNTY MEDICAL SOCIETY

The Philadelphia County Medical Society will hold its Fourteenth Annual Postgraduate Institute at the Bellevue-Stratford Hotel in Philadelphia April 25-28. Among the subjects to be covered will be pediatrics, virus diseases of the skin, antibiotics and chemotherapy, management of inoperable cancer, rehabilitation, carcinoma of the prostate, problems of adolescence, epilepsy, gastrointestinal hemorrhages, obstetric and gynecologic problems, geriatrics, fractures and arthritis. There will also be two special evening sessions at the hotel one consisting of a clinicopathological conference and the other dealing with problems of alcoholism.

Arrangements are being made to record the material presented in the question-and-answer period following each lecture, and a summary of this material will be made available to each paid registrant. The registration fee is $10, payable in advance or at the time of registration. The usual variety of high-grade technical exhibits will be part of the meeting. Preliminary programs have already been mailed to all physicians in Pennsylvania, New Jersey, Delaware, Maryland, and the District of Columbia, but additional copies may be obtained from Gilson Colby Engel, M.D., Director, Philadelphia County Medical Society, 301 South Twenty-First Street, Philadelphia, Pennsylvania.

OPPORTUNITIES FOR MEDICAL PERSONNEL IN THE PACIFIC ISLANDS

Administrative responsibility for Guam and American Samoa, which are United States possessions, and for the Trust Territory of the Pacific Islands, which comprises the former Japanese mandated Marshall, Caroline and Marianas islands, will be transferred from the Navy Department to the Department of the Interior, effective on Guam on July 1, 1950, and in American Samoa and the Trust Territory on July 1, 1951.

Medical work in these islands, in view of the great need for health services, the varied nature of medical problems and the differing cultures of the people, offers an important challenge to doctors and other medical personnel. In establishing medical positions for the governments of these three areas, the Department of the Interior will follow federal classifications, but applicants need not be on a Civil Service register to be eligible for appointment. Positions for physicians, public-health officers, hospital administrators, laboratory technicians, pharmacy technicians and nurses are available. Salaries for doctors will range from $6400 to $8800 per annum. A post differential of 25 per cent in addition to salary is allowed at present for employees stationed in the islands.

Further information regarding opportunities for health work in the Pacific Islands can be obtained from the Division of Territories and Island Possessions, Department of the Interior, Washington 25, D. C.

CLINICAL FELLOWSHIPS IN RHEUMATIC DISEASES

The New England Chapter of the Arthritis and Rheumatism Foundation is sponsoring clinical fellowships for the study of clinical manifestations and management of arthritis and allied diseases to physicians practicing, or intending to practice, in New England. The purpose of the fellowships is the advancement of the knowledge of rheumatism.

Participation in staff work by assignment to various arthritis clinics in Boston will be arranged, the duration of appointment being three to twelve months. From $300 to $500 per month, according to the needs and qualifications of the fellow, will be the stipend.

Applicants must be graduates of a class A medical school in the United States who have completed at least one year of internship at an accredited hospital. They must either be licensed to practice in Maine, New Hampshire, Vermont or Massachusetts, or be acceptable to the Arthritis Committee of the medical society in one of these states. Applicants must be acceptable to the teaching hospitals to which they are assigned and must declare in writing their intent to practice in the New England area for at least two years after completion of the fellowship.

Applications should be addressed to the committee on arthritis of the state medical society or to Dr. Hans Waine, medical director, New England Chapter, Arthritis and Rheumatism Foundation, 201 Devonshire Street, Boston, Massachusetts.

SOCIETY MEETINGS AND CONFERENCES

October 3–May 19. Massachusetts Department of Mental Health. Postgraduate Seminar in Neurology and Psychiatry. Page 286, issue of August 18.

January 9–December 1. Laboratory Courses at Communicable Disease Center, Atlanta, Georgia. Page 950, issue of December 8.

March 4–29. Springfield Hospital Educational Program. Page 347, issue of March 2.

March 10. Public Seminar in Chemotherapy. Page 270, issue of February 16.

March 14. New England Society of Anesthesiologists. Page 234, issue of February 9.

March 14. Boston City Hospital House Officers' Association. Page 348, issue of March 2.

March 14. Massachusetts Physicians Club. Page 385.

March 15. Beth Israel Hospital Lecture. Page 270, issue of February 16.

March 16. Greater Boston Medical Society. Page 385.

March 17 and 18 (note change of dates). New England Health Education Association. Page 305, issue of February 23.

March 20. Hartford Medical Society. Notice above.

March 21. South End Medical Club. Page 385.

March 22. Beth Israel Hospital Lecture. Page 270, issue of February 16.

March 23. Cornell Alumni Day. Page 234, issue of February 9.

March 24. Public Seminar in Chemotherapy. Page 270, issue of February 16.

March 24. Society of American Bacteriologists, Northeast Branch. Page 385.

March 29. Beth Israel Hospital Lecture. Page 270, issue of February 16.

April 3. New England Cardiovascular Society. Page 724, issue of November 3.

April 3. Hartford Medical Society. Notice above.

April 7. Public Seminar in Chemotherapy. Page 270, issue of February 16.

April 13. The Value of the Bone Bank. Dr. Joseph H. Shortell. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

April 17. Boston Lying-in Hospital Obstetric Round Table. Page 888, issue of December 1.

April 17. Hartford Medical Society. Notice above.

April 22–29. American Association of Industrial Physicians and Surgeons. Page 305, issue of February 23.

April 24–28. National Tuberculosis Association. Page 678, issue of October 27.

April 25–28. Philadelphia County Medical Society. Notice above.

April 26. New England Obstetrical and Gynecological Society. Rhode Island Hospital and Providence Lying-in Hospital, Providence, Rhode Island.

April 29. Eastern Section of American Congress of Physical Medicine. Page 306, issue of February 23.

April 29. Long Island College of Medicine Alumni Day. Page 348, issue of March 2.

May 3. Norfolk District Medical Society Anniversary Dinner.

May 4. Suffolk District Censors' Meeting. Page 234, issue of February 9.

(*Notices concluded on page xvii*)

NOTICES (*Concluded from page 386*)

MAY 14–19. International and Fourth American Congress of Obstetrics and Gynecology. Page 160, issue of January 26.

MAY 16–18. Massachusetts Medical Society. Annual Meeting. Hotel Statler, Boston.

MAY 17. Luncheon Meeting. Section on Diseases of the Eye, Ear, Nose and Throat, Massachusetts Medical Society. Hotel Statler, Boston. 12:00 m.

MAY 24–26. American Association of Genito-Urinary Surgeons. Page 234, issue of February 9.

JUNE 22–25. American College of Chest Physicians. Page 270, issue of February 16.

JUNE 24 AND 25. American Society for the Study of Sterility. Page 38, issue of January 5.

JULY 17–22. International Congress for Scientific Research. Page xvii, issue of September 1.

AUGUST 21–26. International Society of Hematology. Page 888, issue of December 1.

AUGUST 31–SEPTEMBER 7. World Federation for Mental Health. Page 306, issue of February 23.

SEPTEMBER 3–9. International Heart Congress. Page 160, issue of January 26.

SEPTEMBER 27–29. Mississippi Valley Medical Society. Page 991, issue of December 15.

NOVEMBER 1. New England Obstetrical and Gynecological Society. Hotel Somerset, Boston.

DISTRICT MEDICAL SOCIETIES

NORFOLK

MARCH 28.
MAY 3. Anniversary Dinner.

SUFFOLK

MAY 4. Censors' Meeting.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, MARCH 16

THURSDAY, MARCH 16

8:15 p.m. Greater Boston Medical Society. Auditorium, Beth Israel Hospital.

FRIDAY, MARCH 17

*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.
*1:30 p.m. Tumor Clinic. Out-Patient Department, Mount Auburn Hospital, Cambridge.

MONDAY, MARCH 20

*11:30 a.m.–12:15 p.m. Chest X-Ray Conference. South End Health Unit, 57 East Concord Street, Boston. Dr. Cleaveland Floyd in charge.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

TUESDAY, MARCH 21

*12:00 m. Luncheon Meeting. South End Medical Club. Headquarters, Boston Tuberculosis Association, 554 Columbus Avenue, Boston.
*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.
*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

WEDNESDAY, MARCH 22

*11:00 a.m.–12:00 m. Medical Rounds. Children's Medical Center.
*12:00 m. Clinical Conference. Margaret Jewett Hall, Mount Auburn Hospital, Cambridge.
*12:00 m.–1:00 p.m. Clinicopathological Conference (Children's Medical Center). Amphitheater, Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Combined Clinic of all Medical Center Services. Amphitheater, Children's Hospital.
*7:30 p.m. Electrolyte Imbalance of Diabetic Ketosis. Dr. Allan M. Butler. Beth Israel Hospital.

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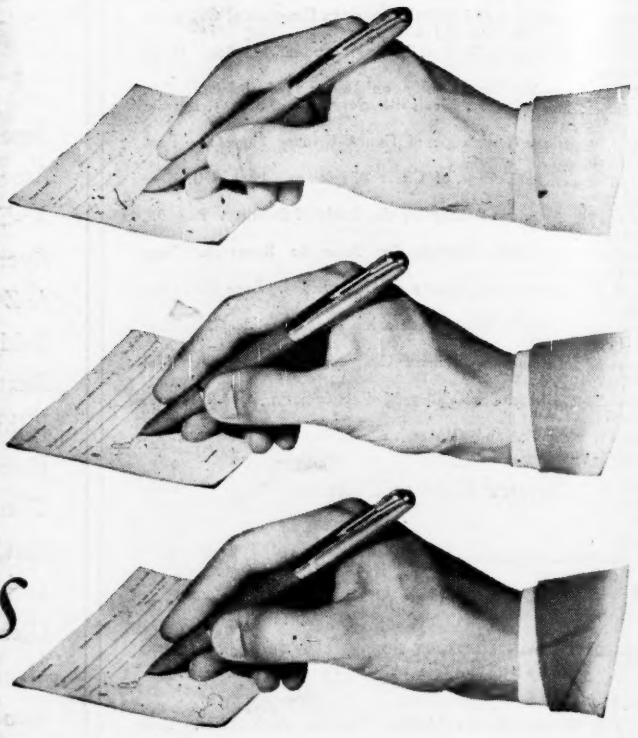

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